ON THE SYNTHESES OF SOME TRITHIENYL METHANES AND TRITHIENYLMETHYL CARBENIUM IONS

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Abstract Several methods for the preparation of tris(thienyl)methanes and trithienylmethyl carbenium ions have been modified. Tris(2-thienyl)methane was prepared through the condensation of thiophene and 2-thiophene aldehyde in the proportions of 2:1 using a catalytic amounts of 70% sulfuric acid at 50 °C. Alternatively catalytic amounts of sulfuric acid absorbed on silica gel were used. The scope of the reaction of 2,5-dialkyl-3-thienyllithium derivatives with alkyl carbonates and methyl chloroformate for the preparation of tris(thienyl)carbinols has been studied. Tris(thienyl)carbenium ions were conveniently prepared through the reaction of tris(thienyl)methanes with trityl perchlorate in anhydrous dichloromethane.

Introduction

In connection with our interest in the spectroscopic and chemical properties of various substituted tris(thienyl)methane derivatives and the carbenium ions, carbanions and radicals derived from them [1] , we have undertaken an investigation of the synthesis of these types of compounds. We have recently described methods for the preparation of tris[2,5-bis(methylthio)-3-thienyl]carbinol, tris[4,5-bis(methylthio)-2-thienyl)carbinol] and tris[2,4,5-tris(methylthio)-3-thienyl]carbinol [2]. Recently also the two isomeric tris(trichlorothienyl)methyl radicals have been prepared from the tris (trichlorothienyl)carbinols *via* the corresponding carbenium ions and studied by EPR-spectroscopy [3].

Very few tris(thienyl)methane derivatives have been described previously. Hartough mentioned in his monograph, as unpublished work, that he obtained tris(5-methyl-2-thienyl)methane by condensation of 2-methylthiophene with 5-methyl-2-thiophene aldehyde in the presence of activated clays at the reflux temperature of toluene [4]. Tris(2-thienyl)carbinol, the derivative, which was first prepared, was obtained by the addition of 2-thienylmagnesium halide to ethyl thiophene-2-carboxylate [5], but was at that time not obtained in pure form.

Another Friedel-Crafts type approach, consisting in the reaction of chloroform with 2-acetylthiophene in the presence of excess of aluminium chloride, gave solely tris(5-acetyl-3-thienyl)methane [6]. These results were confirmed by Meth-Cohn, who also found that this compound gave 2:1 clathrates with a variety of organic compounds [7]. Their structure has been studied by X-ray crystallography [8-11].

In recent years the activity in this field has markedly increased and a number of papers on the synthesis and reactivity of bis(heteroaryl)- and tris (heteroaryl)methane derivatives have appeared. The condensation of 2-methylfuran and 2-methylthiophene with a variety of aldehydes using macropourus ion-exchange resins as catalyst gave high yields of triaryl substituted methanes [12]. Treatment of *N*-(α-benzotriazolyl)alkylcarbamate, available from the condensation of benzotriazole, an aldehyde and an alkyl carbamate or methylfuran in the presence of zinc chloride with excess methylthiophene, was used for the preparation of bis(heteroaryl)alkyl or phenyl methanes [13]. The interest in these compounds was motivated by their potential use as flavour agents of interest for the perfume industry.

Regioselective lithiation of di(2-thienyl)methane at the methylene group has recently been used for the preparation of various trisubstituted methanes [14]. Similarly carbanion reactions at the bridge position of 5,5'-disubstituted di(2-thienyl)methanes have been used [15]. The reaction of 3,4,5-trichloro-2-thienyllithium with acetone has been used for the preparation of dimethyl-3,4,5-trichloro-2-thienylcarbinol and with aldehydes various trichloro-2-thienylcarbinols were obtained. Upon reaction with *p*-toluenesulfonic acid compounds with styryl and phenyl groups underwent a new type of elimination with rearrangement producing thiolactones in high yields [16].

Most interest has been focused on the physical properties and reactions of the trithienyl carbocations. Detailed NMR studies of the tris(2-thienyl) methane cation have been undertaken [17-20]. The structure of the perchlorate has been determined by X-ray crystallography. It was found that the ion is stabilized by delocalization over a conjugated polymethine framework [21]. Nakayama and coworkers have recently published important work on the reaction of this carbenium ion with hydrogen and carbon nucleophiles, which affords three types of addition products, formed by the addition of the nucleophiles to the carbenium ion center and the 3- and 5-positions of the 2-thienyl group [22]. These investigations were extended to an investigation of 2,5-biscarbenium salts [23]. Such compounds were obtained through the reaction of 2,5-dilithiothiophene and di(2-thienyl) ketone and are synthetic precursors for low band gap polymers [24,25]. Also 2,5-biscarbenium ions derived from 2,2'-bithienyl, which are perthienyl analogues of Chichibabin's hydrocarbon, have been studied [26]. They also studied the reaction of the carbanion of tris(2-thienyl)methyllithium with various alkyl halides. With primary alkyl halides only alkylation at the carbanionic center was obtained, whereas with secondary and tertiary alkyl halides in addition alkylation at the 3-position of the thiophene ring was observed [27]. Starting from 2-methyl-4-bromothiophene they prepared tris(5-methyl-3-thienyl)carbinol through halogen-metal exchange at -78 °C followed by reaction with diethyl carbonate. This compound was transformed to the carbenium ion, which was methylated at the carbenium center with methyl magnesium iodide. Upon bromination and halogen-metal exchange, reaction with diethyl carbonate gave a heterotriptycene [28]. Photochemical reactions of diphenyl-2-thienyl carbinol have been studied [29].
An investigation on the EPR-spectra of tris(trithienyl)methyl radicals has been published [30] and re-

cently a study of the dimerization of the diphenyl-2-thienylmethyl radical has been reported [31].

Experimental

Melting points are uncorrected. The ^{1}H NMR spectra were recorded on a Varian XL-300 spectrometer and deuteriochloroform was used as solvent. The mass spectra were recorded on a JEOL-SX 102 spectrometer. The UV spectra were recorded with an UNICAM SP. 800 Ultraviolet spectrophotometer. Column chromatography was carried out with Merck silica gel 60.

Tris(2-thienyl)methane (1a).

To a stirred mixture of 11.2 g (0.10 mol) of 2-thiophenealdehyde [32] and 25.2 g (0.30 mol) of thiophene 3.0 ml of 70% sulfuric acid was added dropwise at room temperature. After one hour the reaction mixture was warmed to 50 °C and stirred for another three hours. At room temperature the crude product was triturated four times with hot ethanol. The combined ethanol fractions were evaporated and the residue chromatographed using first petroleum ether and then petroleum ether/ethyl acetate (9:1) as eluent. The yield of the title compound, obtained as white crystals, was 10.0 g (38%), mp 54 °C (hexane) (lit. [27] mp 54 °C).

2,5-Bis[di(2-thienyl)methyl]thiophene (3).

This compound was obtained from the most polar fractions in the procedure described above, 2.64 g (6%) as orange crystals mp 77-78 °C (hexane); ^{1}H NMR: δ 7.22 (dd, 4H, H5, J = 4.75, 1.65 Hz), 6.94 (m, 8H), 6.76 (S, 2H), 6.04 (s, 2H); MS: M/z 440 (M^+). Anal. Calcd. for $C_{22}H_{16}S_5$: C, 59.95; H, 3.65; S, 36.38. Found: C, 60.05, H, 3.66; S, 36.29.

Tris(5-methyl-2-thienyl)methane (1b).

This compound was prepared according to Chavez and Godinez [33] from 12.6 g (0.10 mol) of 5-methyl-2-formylthiophene[32] , 19.6 g (0.20 mol) of 2-methylthiophene [34] and 3.0 g of acidic silica gel in 50 ml of benzene. The reaction mixture was warmed to 60 °C and 11.0 g (0.078 mol) of phosphorous pentoxide was added over a period of one hour. After stirring for another three hours at the same temperature the solid material was removed by fitration and washed with dichloromethane. The combined filtrates were washed with 10% sodium hydroxide solution and water. After drying over magnesium sulfate and evaporation the residue was chromatographed using petroleum ether as eluent. 11.9 g (39%) of the title compound was obtained as colorless crystals mp 66-67 °C (ethanol); ^{1}H NMR: δ 6.70 (d, 3H, J = 3.25 Hz), 6.57 (d, 3H, J = 3.25 Hz), 5.82 (s, 1H), 2.52 (s, 9H).

Tris(5-bromo-2-thienyl)methane (1c).

To a mixture of 7.86 g (0.030 mol) of 1a in 70 ml of ether and 9.2 ml of 30% hydrogen peroxide cooled to -15 °C, 30 ml of 47% hydrobromic acid was added dropwise during one hour. When the addition was completed the stirring was continued for another two hours and the temperature was kept below -5 °C. At room temperature the phases were separated and the organic phase was washed with saturated sodium chloride solution, 10% sodium hydroxide solution and water. After drying over magnesium sulfate and evaporation the residue was recrystalized first from petroleum ether (80-100 °C) and then from ethanol mp 81-82 °C. The yield of the title compound as colorless crystals was 8.1 g (54%). ^{1}H NMR: δ 6.91 (d, 3H, H4, J = 3.80 Hz), 6.68 (dd, 3H, H3, J = 3.80, 0.90 Hz), 5.81 (s, 1H, methine-H, J = 0.90 Hz); ^{13}C NMR: δ 146.8, 129.6, 126.8, 112.3, 43.3; Anal. Calcd. for $C_{13}H_{7}Br_{3}S_{3}$: C, 31.28; H, 1.41; S, 19.27. Found: C, 31.34; H, 1.43; S, 10.39.

Tris(2,5-dimethyl-3-thienyl)methane (2a).

This compound was prepared as described for **1a** from 14.0 g (0.10 mol) of 2,5-dimethyl-3-formylthiophene[35] and 22.4 g (0.20 mol) of 2,5-dimethylthiophene [36]. The title compound was obtained as white crystals in a yield of 14.5 g (42%); mp 143-144 °C; ^{1}H NMR: δ 6.28 (s, 3H), 5.07 (s, 1H), 2.34 (s, 9H), 2.18 (s, 9H); ^{13}C NMR: δ 139.1, 134.4, 130.2, 126.8, 30.9, 15.3, 12.9.

Anal. Calcd. for $C_{19}H_{22}S_{3}$: C, 65.84; H, 6.39; S, 27.76. Found: C, 65.92; H, 6.46; S, 27.67.

Tris(5-acetyl-2-bromo-3-thienyl)methane (2b).

To a suspension of 33.4 g (0.25 mol) of aluminum trichloride in 70 ml of chloroform 20.5 g (0.10 mol) of 2-acetyl-5-bromothiophene [37] was added in portions at room temperature. The reaction mixture was refluxed over night and then carefully poured into ice-cold 1 M hydrochloric acid. The phases were separated and the water phase extracted with chloroform. The combined organic phases were washed with water, dried over magnesium sulfate and evaporated. The residue was purified by HPLC using a preparative polygosil column (10x500 mm) and heptane/ethyl acetate (9:1) as eluent. The title compound, 7.0 g (34%), was obtained as colorless crystals mp 181-182 °C (ethanol). IR (potasium bromide): ν 1650 cm^{-1} (C=O); ^{1}H NMR: δ 8.13 (s, 3H), 6.42 (s, 1H), 2.55 (s, 9H).

HRMS calcd. for $C_{19}H_{13}Br_{3}O_{3}S_{3}$: 621.7576. Found: 621.7578.

Di(5-acetyl-2-chloro-3-thienyl)chloromethane (4).

This compound was formed in the procedure described above from 16.1 g (0.10 mol) of 2-acetyl-5-chlorothiophene [37]. The title compound,2.6 g (14%), was obtained as colorless crystals mp 140-141 °C (ethanol). IR (potassium bromide): ν 1655 cm^{-1} (C=O); ^{1}H NMR: δ 7.62 (s, 2H), 6.21 (s, 1H), 2.52 (s, 6H).

HRMS calcd. for $C_{13}H_{9}Cl_{3}O_{2}S_{2}$: 365.9109. Found: 365.9116.

Tris(2,5-dimethyl-3-thienyl)carbinol (5).

To a solution of 3.57 g (15.0 mmol) of 3-iodo-2,5-dimethylthiophene [38] in 80 ml of anhydrous ether 8.0 ml of 2.02 M butyllithium was added dropwise under nitrogen at -78 °C. The reaction mixture was stirred for 15 min and then 3.75 g (15.0 mmol) of di(2,5-dimethyl-3-thienyl)ketone [39] in 30.0 ml of anhydrous ether was added dropwise. After stirring for three hours at -78 °C the cooling bath was removed and the reaction left over night. The reaction mixture was poured into ice-cold saturated ammonium chloride solution. The phases were separated and the organic phase washed with water, dried over magnesium sulfate and evaporated. The solid residue was triturated with two 5 ml portions of pentane. After recrystallization from ethanol 3.69 g (68%) of the title compound was obtained as white crystals, mp 110-111 °C (decomp.). IR (potassium bromide): ν 3600 cm^{-1}; ^{1}H NMR: δ 6.46 (s, 3H), 2.19 (s, 18H); MS: m/z 362 (M$^+$).

Anal. Calcd. for $C_{19}H_{22}OS_3$: C, 62.93; H, 6.11; S, 26.53. Found: C, 62.95; H, 6.08; S, 26.55.

Di(2,5-di-*t*-butyl-3-thienyl)ketone (6).

To a cooled solution of 4.13 g (15.0 mmol) of 3-bromo-2,5-di-*t*-butylthiophene [40] in 100 ml of anhydrous ether at -78 °C under nitrogen was treated with 8.0 ml of 2.02 M butyllithium in cyclohexane and stirred for 30 min., after which 0.45 g (5.00 mmol) of dimethyl carbonate in 3.0 ml of anhydrous ether was slowly added. The reaction mixture was stirred for 4 h at -78 °C and then allowed to warm to room temperature overnight. The reaction mixture was quenched with ice-cold saturated ammonium chloride solution. The organic phase was dried over magnesium sulfate and evaporated. The solid residue was recrystallized from ethanol giving 1.03 g (35%) of the title compound as white crystals mp 218-219 °C (lit. [39] mp 221-222 °C).

1,3,5,7-Tetra-*t*-butylbenzo[1,2-*c*;4,5-*c'*]dithiophene-4,8-dione (7).

When 5.31 g (15.0 mmol) of 3,4-dibromo-2,5-di-*t*-butylthiophene [40] was used as in the procedure described for **6**, 0.60 g (19%) of the title compound was after sublimation at 192-194 °C/9mm Hg obtained as white crystals. IR (potassium bromide): ν 1650 cm^{-1} (C=O); ^{1}H NMR: δ 1.57 (s); MS: M/z 444 (M$^+$).

Anal. Calcd. for $C_{26}H_{36}O_2S_2$: C, 70.22; H, 8.16; S, 14.42. Found: C, 70.03; H, 8.15; S, 14.42.

Reduction of tris(thienyl)carbinols to tris(thienyl)methanes.

To a mixture of 0.25 ml (2.0 mmol) of trimethylsilyl chloride, 0.75 g (5.0 mmol) of sodium iodide and 15 ml of acetonitrile 2.0 mmol of the carbinol was added. The reaction mixture was stirred in the dark at room temperature over night. After addition of sodium thiosulfate solution the product was extracted with two 15 ml portions of diethyl ether. The combined ether phases were dried over magnesium sulfate and evaporated. The residue was recrystallized from hexane.

Tris(2-thienyl)carbinol [17] gave 0.43 g (82%) of a compound identical with **1a** described above.

Tris(5-methyl-2-thienyl)carbinol [17] gave 0.53 g (87%) of a compound identical with **1b** described above.

Tris(2,5-dimethyl-3-thienyl)carbinol (**5**) gave 0.63 g (91%) of a compound identical with **2a** described above.

Preparation of tris(thienyl)methyl perchlorate.

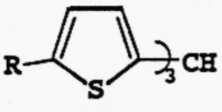
To a solution of 0.34 g (1.0 mmol) of freshly prepared trityl perchlorate [41] in 3.0 ml of anhydrous dichloromethane 1.0 mmol of the tris(thienyl)methane was added. The reaction mixture was stirred over night under nitrogen at room temperature. Upon careful trituration with about 3 ml of petroleum ether colored crystals were formed. Most of the liquid was removed by decantation and the rest with a pipette. The remaining crystals were washed with pentane/ether (4:1) followed by drying *in vacuo* at room temperature.

Tris(2-thienyl)methane (**1a**) gave 0.22 g (62%) of **8a** as brown-red crystals, mp 155-156 °C. MS (EI): m/z 260 (M^+-1-ClO_4).

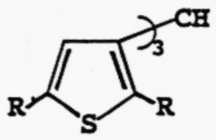
Tris(5-methyl-2-thienyl)methane (**1b**) gave 0.31 g (77%) of **8b** as red crystals mp 166-167 °C; UV (acetonitrile): λ_{max} (log ε) 233 (2.31), 282 (2.36); ^1H NMR: δ 8.03 (d, 3H, J = 4.0 Hz) 7.48 (d, 3H, J = 4.0 Hz), 2.82 (s, 9H); ^{13}C NMR: δ 169.5, 147.2, 139.8, 133.5, 17.7; MS (EI): m/z 302 (M^+-1-ClO_4).

Results and discussion

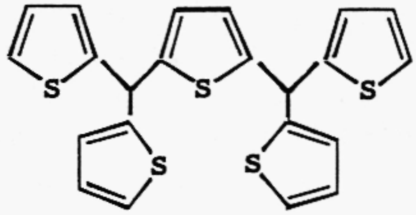
In the present work we could prepare the parent tris(2-thienyl)methane through the condensation of 2-thiophene aldehyde and thiophene in the proportion of 1:2 using a catalytic amount of 70% sulfuric acid at 50 °C. Extraction of the reaction product with hot ethanol followed by column chromatography using light petroleum as eluent gave tris(2-thienyl)methane (**1a**) in 38% yield and 2,5-di-(di-2-thienylmethyl)thiophene (**3**) in 6% yield. Recently Nakayama and coworkers prepared **1a** in 33% yield using phosphorus pentoxide in benzene as condensing agent [27]. We found that using only phosphorus pentoxide gave lower yields and that in certain cases no reaction occurred. In the preparation of tris(5-methyl-2-thienyl)methane (**1b**) and tris(2,5-dimethyl-3-thienyl)methane (**2a**) we used catalytic amounts of sulfuric acid adsorbed on silica gel following a recently introduced method [33], and **1b** and **2b** were obtained in 39% and 34% yield, respectively. Bromination of **1a** with hydrogen bromide and hydrogen peroxide gave tris(5-bromo-2-thienyl)methane (**1c**) in 54% yield.



1
a R=H
b R=CH_3
c R=Br

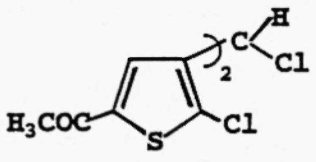


2
a R=R=CH_3
b R=Br,R'=$COCH_3$

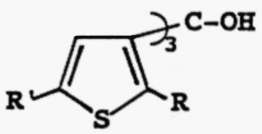


3

Applying the method of Gol'dfarb *et al.* [42] to 2-acetyl-5-chlorothiophene, the reaction failed and we obtained di-(5-acetyl-2-chloro-3-thienyl)methyl chloride (**4**) in 14% yield. On the other hand the



4

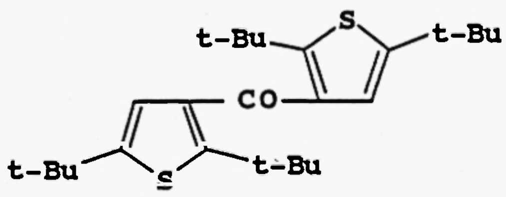


5

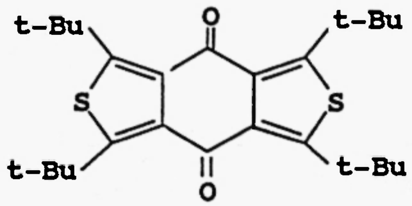
R=R'=CH_3

reaction of 2-acetyl-5-bromothiophene with chloroform-aluminum chloride in the proportion of 1:2 gave tris(5-acetyl-2-bromo-3-thienyl)methane (**2b**) in 34% yield.

We also investigated the scope of the reaction of 2,5-dialkyl-3-thienyllithium derivatives with dimethyl- or diethyl carbonate or methyl chloroformate in the proportion of 3:1 in order to obtain the carbinols. Metal-halogen exchange between 3-iodo-2,5-dimethylthiophene with butyllithium followed with 1/3 equivalent of methyl carbonate gave tris(2,5-dimethyl-3-thienyl)carbinol (**5**) in only 23% yield. Better yields of **5** (68%) were obtained in the reaction of 2,5-dimethyl-3-thienyllithium and di-(2,5-dimethyl-3-thienyl)ketone. We then turned to sterically more crowded systems. Reaction of di-(2,5-di-*t*-butyl-3-thienyl)lithium with 1/3 of an equivalent of dimethyl carbonate stopped at the di-(2,5-di-*t*-butyl-3-thienyl) ketone (**6**), which was obtained in 35% yield.



6



7

Upon halogen-metal exchange of 3,4-dibromo-2,5-di-*t*-butylthiophene with one equivalent of butyllithium and reaction with dimethyl carbonate only the quinoid 1,3,5,7-tetra-(*t*-butyl)benzo-[1,2-c;4,5-c']dithiophene-4,8-dione (**7**) was obtained in 9% yield probably due to competing dilithiation reaction. In both cases no traces of carbinols could be found. Tris(2-thienyl)carbinol, tris(5-methyl-2-thienyl)carbinol [20] and **5** could easily and in high yields be reduced to the tris(2-thienyl)methane derivatives **1a** and **1b** and tris(2,5-dimethyl-3-thienyl)methane (**2a**) using trimethylsilyl chloride and sodium iodide in acetonitrile.

Tris(thienyl)methyl carbenium perchlorates have previously been prepared from the corresponding carbinols by treatment with 60% aqueous perchloric acid in acetic anhydride [21,28,30,43]. We found it more convenient to allow the tris(thienyl)methane derivatives to react with trityl perchlorate in anhydrous dichloromethane. In this way we obtained tris(2-thienyl)methylcarbenium perchlorate (**8a**) and tris(5-methyl-2-thienyl)methyl carbenium perchlorate (**8b**) in pure form in 62% and 77% yield, respec-

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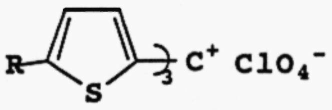
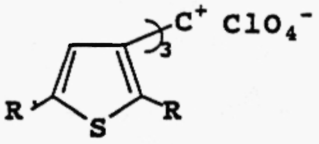


8

a $R=H$
b $R=CH_3$
c $R=Br$



9

$R=R'=CH_3$

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