

Thiophene Analogues of Fluorene

V. Competitive Metalations of Some Tetramethylcyclopentadithiophenes, Fluorene and 3-Methylfluorene*

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Competitive metalation of 1,3,4,6-tetramethyl-7H-cyclopenta[1,2-c:3,4-c']dithiophene (Ib), 2,3,4,6-tetramethyl-7H-cyclopenta[1,2-b:3,4-c']dithiophene (IIb), 2,3,4,5-tetramethyl-7H-cyclopenta[1,2-b:4,3-b']dithiophene (IIIb), fluorene (VII), and 3-methylfluorene (VIII) with ethereal ethyl lithium has been carried out. The relative rates of metalation of Ib:IIb:VIII:VI:IIIb were found to be 1:16.8:371:754:1360. Factors determining the relative metalation rates and acidities of tetramethylcyclopentadithiophenes are discussed.

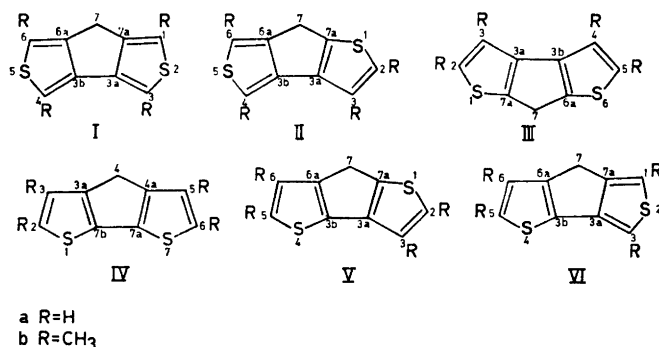
During recent years, work has been in progress in this Laboratory concerning the effect of annelating aromatic rings on the *b* side and *c* side of thiophene on the chemical and physical properties.^{1,2} The markedly different chemistry of benzo[*b*]thiophene and benzo[*c*]thiophene prompted us to investigate this annelating effect closer.³

Cyclopentadithiophenes are a rather new class of heterocyclic compounds, which can be considered as thiophene analogues of fluorene. There are six isomers (I–VI) in which the thiophene rings are annelated with either their *b* side or *c* side, or both. In these cyclopentadithiophenes, the carbocyclic ring can formally be considered as a cyclopentadiene ring (three isomers), as a cyclopentene ring (two isomers), and as a cyclopentane ring (one isomer). Quite different chemical and physical properties can be expected for these three principally different classes of cyclopentadithiophenes. All the parent compounds (Ia–VIa) have recently been synthesized by Wynberg and coworkers.^{4–6}

In our Laboratory, we chose to study the four tetramethyl-substituted derivatives Ib–IVb, the synthesis of which has been described in an earlier

* Taken in part from the Ph.D. thesis of A. K. Wiersema, University of Groningen, the Netherlands, 1970.

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paper.⁷ We selected the tetramethyl derivatives, because we believed on the basis of previous results⁸ that they could be synthesized more easily than the parent compounds. However, this proved to be true only for Ib. Since we wanted to study the metalation reactions of these compounds, the methyl groups were advantageous as the acidic thiophenic α -hydrogens could interfere in the metalation reaction. That this is possible has recently been demonstrated by MacDowell and Jeffries,⁹ who found that 8H-indeno[1,2-c] thiophene is metalated by butyl lithium at the CH₂ group as well as both thiophenic α -positions.

We have earlier shown that the ketones (fluorenone analogues) corresponding to Ib – IVb react differently on reduction with lithium aluminum hydride-aluminum chloride⁷ and also give quite different results upon reaction with dienophiles.^{10,11} We especially expected the acidity of the CH₂ group to be very sensitive to the mode of annelation.⁸

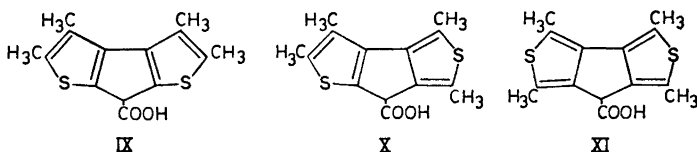
During recent years, the study of the acidity of hydrocarbons has received much attention. Different approaches have been used and are reviewed in a number of books and papers.^{12–16} Streitwieser and coworkers, using the cyclohexylamine-lithium cyclohexylamide system and UV spectroscopic technique, have determined thermodynamic acidities for a large number of weak carbon acids.^{17–19} Although Janssen and de Jong²⁰ have measured the UV spectrum of some of the anions of Ia – VIa, we were not successful in applying the Streitwieser technique to Ib – IVb. We therefore turned to a study of the kinetic acidity.

The kinetic acidity is often determined by measuring the hydrogen-deuterium^{19,21,22} or hydrogen-tritium exchange^{22,23} of the carbon acids with appropriate bases. When the carbon acids are closely related and their acidity only spans a few pK_a units, the Brønsted relation can be used to relate kinetic acidity to thermodynamic acidity.^{12,13}

In the present paper we present the results of some competitive metalations of Ib – IIIb with ethereal ethyl lithium, which were used to determine kinetic acidities. Fluorene (VII) and 3-methylfluorene (VIII) were used to bridge the reactivity gap between Ib and IIb.

A mixture of two of these hydrocarbons was metalated with an insufficient amount of ethyl lithium and then carbonated. Carbonation is a widely used

method for determining the composition of a mixture of anions (*cf.* Refs. 12, 13, 24). Usually such mixtures of carboxylic acids are analyzed *via* their methyl esters by VPC technique. However, this method was not useful in our case, since the esterification of 7-carboxy-2,3,4,5-tetramethyl-7H-cyclopenta[1,2-b:4,3-b']dithiophene (IX) with diazomethane formed a mixture of compounds.



In order to apply the same analytical method in all cases, the use of NMR spectroscopy was adopted. The NMR signals due to the four methyl groups in the tetramethylcyclopentadithiophenes are detectable, even at low concentration. Authentic samples of the carboxylic acids IX – XI were prepared *via* metalation and carbonation. The acid XI has been described earlier.⁸ Competitive metalation experiments were carried out between VII and VIII, I Ib and Ib, VIII and I Ib, VII and I Ib, IIIb and VII, and IIIb and I Ib. From the compositions obtained, relative rates were calculated in the usual manner.²⁵ (For details, *cf.* Ph.D. thesis of A. K. Wiersema, University of Groningen, the Netherlands, 1970.) The relative rate of metalation of Ib:IIIb:VIII:VI:IIIb were found to be 1:16.8:371:754:1360. Since the relative rate of metalation of fluorene has been determined in two experiments, we have given it the medium value of two calculated. The value of $k_{\text{VII}}:k_{\text{I Ib}}$ and the combined values of $k_{\text{VII}}:k_{\text{VIII}}$ and $k_{\text{VIII}}:k_{\text{I Ib}}$ differ only by 3 %.

Transmetalation reactions (leading to an equilibrium) were shown to be very slow. When, *e.g.*, fluorene was added to a solution of the lithium derivative of IIIb, it appeared that after carbonation almost exclusively 9-fluorenyl-carboxylic acid had been formed. In the case that IIIb was added to a solution of 9-fluorenyllithium, after carbonation almost exclusively IX had been formed. Reaction times were up to two days. Conant and Wheland²⁴ describe this same feature for a number of their reaction pairs. Equilibrium was sometimes not reached before several weeks.

It is evident that the rate of metalation is very sensitive to the mode of annelation. Compound IIIb with its formal cyclopentadiene ring gives the highest rate of metalation, while Ib with its formal cyclopentane ring gives the lowest.

However, the formal unsaturated nature of the central ring system is certainly not the only factor in determining the acidity of the CH_2 groups. There is ample physical evidence that an electron-donating group conjugates much better from the 2-position than from the 3-position.²⁶ Many more "good" resonance structures can be written for the carbanion from III, delocalizing the charge to the 2, 5, 3a, and 3b positions, than for II and I, in which case delocalization to the 3b-position of II would involve resonance structures with ten electrons around one of the sulfur atoms. Using this reasoning, a lower

acidity and metalation rate would be expected for IV in spite of the formal cyclopentadienic structure of the carbocyclic ring, as even less "good" resonance structures can be written for the carbanion of IV than of II. However, MO-calculation by Janssen and de Jong²⁷ on Ia–VIa indicated that IVa should have a smaller pK_a -value (be more acidic) than IIa, although their calculations clearly indicated that IVa should be the least acidic of the three "cyclopentadienic" analogues. Calculations for the methylated compound would probably give similar results. For the calculation of pK_a -values they used a method suggested by Wheland,²⁸ which assumes that the acidity of the hydrocarbon is proportional to the change in the π -bond energy, resulting from the difference in conjugation between the hydrocarbon and the corresponding anion. This method has also been used by Streitwieser in his calculations.²⁹

The question whether or not a Brønsted relation between metalation rates and thermodynamical pK_a -values can be obtained, is of course still open. However, this seems hardly probable, as other factors may be of importance in determining the rates of metalation for Ib–IIIb. It is generally assumed that in metalation of thiophenes with organolithium compounds, coordination occurs to the sulfur atom, while the carbanion part is attacking an adjacent hydrogen atom.³⁰ This coordination has been considered to be responsible for the exclusive α -metalation of simple thiophenes.³⁰ It is evident that such coordination could facilitate the metalation of IIb and especially IIIb, but be of no importance in the metalation of Ib. Finally steric effects of the methyl groups should be in the same direction and also retard the metalation of I more than of II and especially of III.

EXPERIMENTAL

Materials. Specially purified samples of the tetramethylcyclopentadithiophenes Ib–IIIb were used.⁷ Fluorene was obtained from BDH, and recrystallized from ethanol–water before use. 3-Methylfluorene was prepared by decarboxylation of 9-carboxy-3-methylfluorene, obtained from the $AlCl_3$ -catalyzed reaction of phenylglyoxylic acid and toluene.³¹

7-Carboxy-2,3,4,5-tetramethyl-7H-cyclopenta[1,2-b:4,3-b']dithiophene (IX). To a solution of 1.0 g (4.3 mmol) of 2,3,4,5-tetramethyl-7H-cyclopenta[1,2-b:4,3-b']dithiophene in 100 ml of anhydrous ether, 20 ml of 0.79 N ethereal ethyl lithium was added. The colour turned first orange, but after about 1 min changed to yellow. The mixture was boiled under reflux for 15 min and poured onto carbon dioxide, covered with anhydrous ether. After the usual work-up, the crude product was recrystallized from benzene. This yielded 0.65 g (2.3 mmol) or 53 % of the title compound. Further recrystallization from benzene gave an analytically pure product, m.p. 199–200°C (dec.). The NMR spectrum ($(CD_3)_2SO$) exhibits a methinic proton at τ 5.13 (s,1) and methyl groups at τ 7.62 (s,6) and τ 7.68 (s,6). In C_5D_5N , the methyl groups appear as a singlet at τ 7.73. [Found: C 61.2; H 5.21; S 22.9. Calc. for $C_{14}H_{14}O_2S_2$ (278.4): C 60.40; H 5.07; S 23.03.]

7-Carboxy-2,3,4,6-tetramethyl-7H-cyclopenta[1,2-b:3,4-c']dithiophene (X). 7-Carboxy-2,3,4,6-tetramethyl-7H-cyclopenta[1,2-b:3,4-c']dithiophene was obtained in the same way as described for (IX), in 41 %. The colour of the anion was yellow.

After recrystallizations from benzene, the m.p. was 218.5–219.5°C. The NMR spectrum ($(CD_3)_2SO$) reveals a methinic proton at τ 5.23 (s,1), and methyl groups at τ 7.37 (s,6) and τ 7.65 (s,6). In C_5D_5N , the methyl groups appear as singlets of equal intensity at τ 7.53 and 7.77. [Found: C 60.4; H 5.98; S 22.7. Calc. for $C_{14}H_{14}O_2S_2$ (278.4): C 60.4; H 5.07; S 23.03.]

7-Carboxy-1,3,4,6-tetramethyl-7H-cyclopenta[1,2-c:3,4-c']dithiophene (XI). 7-Carboxy-1,3,4,6-tetramethyl-7H-cyclopenta[1,2-c:3,4-c']dithiophene was made as described by Gronowitz and coworkers⁸ in 58 % yield after recrystallization from benzene, m.p. 247°C (dec.). Lit. value⁸ 242–245°C. The NMR spectrum (C₆D₆N) shows the methyl groups as a singlet at τ 7.54.

7-Carbomethoxy-2,3,4,6-tetramethyl-7H-cyclopenta[1,2-b:3,4-c']dithiophene. 0.22 g (0.80 mmol) of 7-carboxy-2,3,4,6-tetramethyl-7H-cyclopenta[1,2-b:3,4-c']dithiophene was treated with an excess of ethereal diazomethane solution. After evaporation of the ether, the crude product was sublimed (130°C, 10⁻³ mm) and recrystallized from methanol, m.p. 164–165°C. The yield was 0.16 g (68 %). The NMR spectrum (CDCl₃) shows methyl groups at τ 7.47 (s,3) and τ 7.67 (s,9), a carbomethoxy group at τ 6.28 (s,3) and a methinic hydrogen at τ 5.56 (broad, 1). [Found: C 61.6; H 5.54; S 21.9. Calc. for C₁₅H₁₆O₂S₂ (292.4): C 61.6; H 5.52; S 21.93.]

7-Carbomethoxy-1,3,4,6-tetramethyl-7H-cyclopenta[1,2-c:3,4-c']dithiophene. 0.34 g (1.2 mmol) of 7-carboxy-1,3,4,6-tetramethyl-7H-cyclopenta[1,2-c:3,4-c']dithiophene was converted into its methyl ester in the way as described above. The yield was 0.3 g (83 %), m.p. 154.5–155.5°C. The NMR spectrum (CDCl₃) shows methyl groups at τ 7.44 (s,6) and τ 7.73 (s,6), a carbomethoxy group at τ 6.32 (s,3), and a methinic hydrogen at τ 5.63 (broad, 1). [Found: C 61.6; H 5.58; S 21.8. Calc. for C₁₅H₁₆O₂S₂ (292.4): C 61.6; H 5.52; S 21.93.]

The competitive metalation reactions were carried out as is described below for 3-methylfluorene and 2,3,4,6-tetramethyl-7H-cyclopenta[1,2-b:3,4-c']dithiophene. The analysis of the carboxylic acid mixtures was carried out with NMR spectroscopy. Deuteropyridine (C₅D₅N, Ciba) was selected as a suitable solvent. The signals of the methyl groups of the tetramethylcyclopentadithiophenes were used for the analyses. The most suitable signals were chosen from fluorene and 3-methylfluorene, and in cases where the signals had the same chemical shift, this was corrected for in the calculations.

Competitive metalation of 3-methylfluorene and 2,3,4,6-tetramethyl-7H-cyclopenta[1,2-b:3,4-c']dithiophene. A 250 ml three-necked flask was flushed thoroughly with pure nitrogen before the experiment. The experiment itself was carried out in a nitrogen atmosphere.

544 mg (3.19 mmol) of 3-methylfluorene and 700 mg (2.99 mmol) of 2,3,4,6-tetramethyl-7H-cyclopenta[1,2-b:3,4-c']dithiophene was placed in the flask. 125 ml of anhydrous ether was added. The solution was stirred magnetically, 4 ml of 0.70 N (2.80 mmol) ethereal ethyl lithium were added, and the mixture was boiled under reflux for 5 min. The yellow solution was poured onto carbon dioxide, covered with anhydrous ether. Thorough work-up gave 390 mg of a mixture of carboxylic acids.

NMR spectra were obtained with a Varian A60 high resolution spectrometer.

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