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Thiophene Analogues of Indenes

I. The Synthesis of Indanone Analogues

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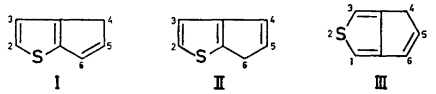
Synthetic routes to 4,5-dihydro-6H-cyclopenta[b]-thiophene-6-ones (IV) and 5,6-dihydro-4H-cyclopenta[b]-thiophene-4-ones (V), being thiophene analogues of 1-indanones, have been investigated. The route through polyphosphoric acid (PPA) cyclization of vinylketones, obtained from the Mannich bases of acylthiophenes was improved.

A one step annelation onto the 2,3-position of thiophenes was discovered in the reaction of thiophene with methacrylic acid in PPA.

The NMR-spectra of the thiophene analogues of 1-indanones are discussed.

The chemistry of indene has been thoroughly investigated since its discovery in 1890 by Krämer and Spilker.[1] In recent years, particularly due to the development of NMR spectroscopy, there has been renewed interest in the tautomeric properties of indene and its derivatives,[2–5] culminating in the discovery of a unique stereospecific tautomerism by Bergson and Weidler.[6,7]

However, the thiophene analogues 4H-cyclopenta[b]thiophene (I), 6H-cyclopenta[b]thiophene (II) and 4H-cyclopenta[c]thiophene (III) or their derivatives appear to be completely unknown. Except for a passing reference



I II III

to a compound that gave the characteristic test of unsaturation and that rapidly deteriorated, no other report concerning their existence has been published.[8]

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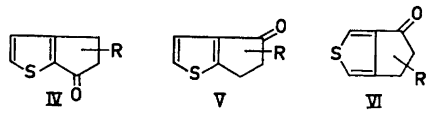
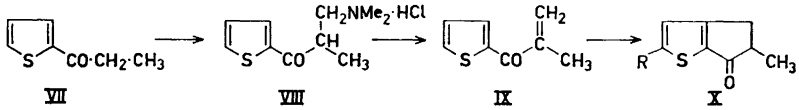
Unlike indene, in which both tautomers are identical, the thiophene analogues (I and II)* are of particular value and interest for tautomeric study. The ease with which thiophenes can be selectively substituted renders a study of the influence of substituents on the equilibrium position and rate of tautomerisation in this series specially attractive. Furthermore the metallation of these indenes (I, II, and III) presents the interesting possibility of competition between two acidic positions, that of the cyclopentadiene ring and the α-position of the thiophene. Finally it is of interest to study the differences in aromatic properties, acidities *etc.*, between the 2,3-annelated systems (I, II) and the 3,4-annelated system (III) (*cf.* Ref. 9).

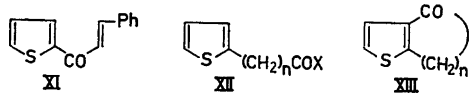
We considered that the most reasonable route to this system lay in the preparation of the ketones (IV, V, VI) which could then be reduced to the alcohols and these dehydrated to indenes.



The first literature report of the preparation of a thiaindanone was that of Burckhalter and Sam,[10] who in 1951 succeeded in cyclising the unsaturated ketone (IX), prepared from the Mannich base (VIII) as shown to give 2-



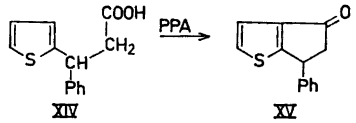
methylthiaindanone-1 (X; R = H). Since then, Sam and Thompson [8] have applied this method to the synthesis of the 5-chloro analogue (X; R = Cl), in an over-all poor yield. Acheson and co-workers [11] have reported the unsuccessful cyclisation of the analogous 2-cinnamoylthiophene XI, using polyphosphoric acid (PPA).



Another route to the ketones IV and V, which in the benzene series yields indanones in almost quantitative yields,[12] is the cyclisation of β-thienylpropionic acids or their acid chloride derivatives. Although the corresponding butyric and valeric acid chlorides (XII; n = 3 or 4, X = Cl) cyclised in high yield [13–17] on treatment with stannic chloride in carbon disulphide to give the corresponding ketone (XIII), when the same workers [17] applied this reaction to the propionyl derivative (XII; n = 2, X = Cl) they obtained only a trace

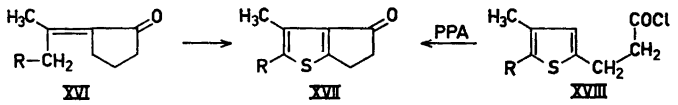
* Sam and Thompson [8] have proposed the name thiaindan for the reduced analogues.

of an unspecified product. However, Acheson and co-workers [11] obtained the ketone (XV) by treatment of the acid (XIV) with PPA in 35 % yield and more recent work by Sam and Thompson [8] using the same reagent yielded the



XIV XV

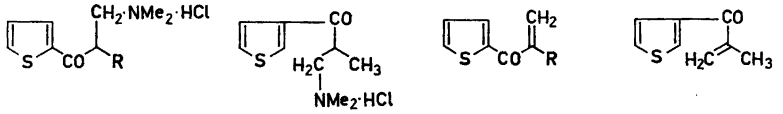
parent indanones (IV and V; R = H) and their 2-methyl and 2-phenyl derivatives in fair yields. The cyclisation only occurred if the acid was treated in an inert solvent (methylene chloride or chlorobenzene) with PPA. In one case they obtained 2-phenyl-thiaindanone-1 from the corresponding acid by treatment with liquid hydrogen fluoride in over 70 % yield. Finally, Poirier [18,19] has reported that the indanone (XVII) is obtained either by treatment of the



XVI XVII XVIII

cyclopentanone (XVI) with sulphur or by PPA treatment of the acid chloride (XVIII). However, no details were given.

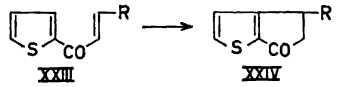
We therefore first set out to reinvestigate the original method of Burckhalter and Sam [10] and to assess its scope and limitations. 2-Thienyl ketones are readily available by acylation of thiophene, while the 3-substituted analogues may be obtained by the method of Gronowitz [20] by way of 3-bromothiophene. By modifying the procedure for the Mannich reaction, according to the suggestions of Mironov and Farberov [21] we were able to obtain the Mannich bases from 2-acetyl (XIX; R = H), 2- (XIX; R = CH_3) and 3-propionyl (XX) and 2-phenacetyl thienyl ketone (XIX; R = Ph) in consistently high yields. Furthermore by heating the base hydrochloride under



XIX XX XXI XXII

high vacuum in the presence of a radical scavenger at 200° we obtained the corresponding vinyl ketones in higher yields than previously reported. However, except for the cyclisation of the 2-and 3-methacryloyl thiophenes (XXI; R = CH_3 and XXII), which gave the corresponding indanones in high yield on treatment with PPA at 35°, the cyclisations were not successful. It appears that the unsubstituted acryloyl thiophene (XXI; R = H) and the phenyl analogue (XXI; R = Ph) (which behaves like styrene) are readily polymerised under acid conditions, this polymerisation being hindered by the presence of an alkyl group.

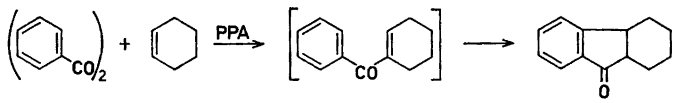
Because of the ease of cyclisation of the 2-methacryloylthiophene (XXI; R = CH_3) to the indanone analogue (X) we considered that treatment of thiophene with methacrylic acid in PPA might give the 5-membered ketone in one step. This in fact was the case, and when the reaction was conducted in methylene chloride solution at 55°, (X; R = H) was obtained in 40 % yield. We therefore extended this reaction to the acylation of thiophene with crotonic β,β-dimethylacrylic, and cinnamic acids in PPA, but in each case isolated in good yield the respective unsaturated ketone (XXIII; R = CH_3, $(CH_3)_2$, and Ph). However, cyclisation to the indanone analogues (XXIV) was accom-



XXIII XXIV

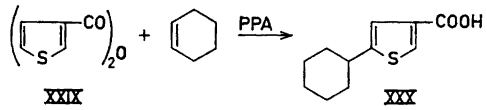
plished by treatment with the same reagent at higher temperatures and for longer times giving the product in good yields. Attempts to form the cyclic ketone in one step from thiophene resulted in very low yields. The remarkable ease with which the methacryloylthiophenes (XXI; R = CH_3 and XXII) cyclised compared with 2-crotonylthiophene (XXIII; R = CH_3) could be due to the favourable configuration of the carbonyl group and the double bond *(trans)* for cyclisation in the former case while the *cis* configuration is preferred in the crotonyl derivative. Infrared data support this suggestion. The difference between the carbonyl and double-bond stretching frequencies is only 20 cm^{-1} in the methacryloyl compound while in the crotonyl derivative it is 45 cm^{-1} and the double bond absorption is stronger than that of the carbonyl suggesting that this structure is *cis*-locked.[22]

In order to make the above type of reaction applicable to both series of indanone derivatives (IV and V) we endeavoured to acylate an olefin with a thiophenecarboxylic acid, thus choosing the site of the carbonyl group. This type of reaction has been achieved in the benzene series [23] and in some cases the indanone derivative was isolated directly. Thus, the hydrofluorenone XXVIII was obtained by way of 1-benzoylcyclohexene (XXVII), when benzoic anhydride and cyclohexene were treated with PPA. However, in the



XXV XXVI XXVII XXVIII

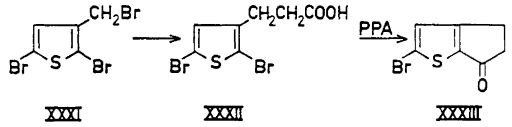
thiophene series an unexpected result was observed. Thus when 3-thenoic anhydride (XXIX) (prepared in quantitative yield by the method of Smalley and Suschitzky [24]) was similarly treated with cyclohexene, 2-cyclohexyl-4-thenoic acid (XXX) was isolated, no ketonic products being obtained. The



XXIX XXX

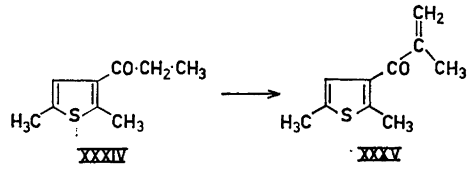
structure was evident from the NMR-spectrum. The thiophenic hydrogen resonances showed the coupling of 1.5 c/s characteristic of 2,4-disubstitution. The greater activity of the thiophene ring over the benzene ring overcame the deactivating effect of the anhydride group and thus reversed the role of the two reagents.

We have also made two preliminary attempts to prepare the unknown indanone system VI. Thus when the propionic acid (XXXII), prepared from 3-methylthiophene by way of reacting the derivative XXXI with ethyl



XXXI XXXII XXXIII

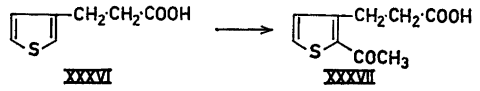
malonate, was heated with polyphosphoric acid we hoped to obtain the dibromo derivative of the 3,4-annelated ketone (VI). However, the ketone obtained (XXXIII), resulted by electrophilic substitution of a bromine atom. Also, when 2,5-dimethylthiophene was treated with methacrylic acid and PPA, only non-ketonic polymeric material was obtained, as also was the case when the ketone (XXXV), obtained by way of the Mannich base from XXXIV as



XXXIV XXXV

mentioned previously, was treated in the usual manner.

During attempts to improve the yield of the PPA catalysed cyclisation of the propionic acid XXXVI by use of various solvents, we found that

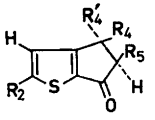


XXXVI XXXVII

acetic acid reacted readily with the system to give the product XXXVII in good yield. NMR-spectrum of the crude product indicated also the presence of smaller amounts of the 5-acetylated product.

The NMR-spectra demonstrate the cyclic nature of the thiophene analogues of the indanones. The data are collected in Table 1. The two thiophenic hydrogens show the coupling constants characteristic of 4,5-disubstituted thiophenes [25] and it can be noticed that substituents in the carbocyclic ring have very little influence on the chemical shifts of the thiophenic hydrogens. The assignment of the thiophene hydrogen bands is based on the known effect of a carbonyl function on the chemical shifts of such hydrogens.[26] The 3-hydrogen resonances are split due to long-range coupling with the hydrogens

Table 1. Chemical shifts (τ-values) and coupling constants (c/s) of 4,5-dihydro-6H-cyclopenta[b]thiophene-6-ones in CCl_4 solution



R_2	R_4	R_4'	R_5	H_2[a]	H_3[a]	R_4[a]	R'_4[a]	H_5[a]	R_5[a]
H	H	H	H	2.15 d (5.0)	2.98 d (4.9)[b]	A_2B_2	pattern centered at		7.05
Br	H	H	H	—	2.93 s	A_2B_2	»	»	7.08
H	Ph	H	H	2.17 d (5.0)	3.14 d (4.9)[c]	2.8[d]	5.51 q (3.3, 7.2)	6.67 q (7.2, 18.8)	7.08 q (3.3, 18.8)
H	H	H	Ph	2.08 d (4.9)	2.95 d (4.9)[b]	6.83 (3.6, 17.4)	6.52 (7.0, 17.4)	5.90 q (3.6, 17.4)	2.8[d]
H	CH_3	CH_3	H	2.08 d (4.8)	2.92 d (4.9)	8.57 s	8.57 s	7.25 s	7.25 s
H	CH_3	H	H	2.07 d (5.0)	2.90 d (5.0)	8.60 d (7.0)	6.3—7.9 m	6.3—7.9 m	6.3—7.9 m
H	H	H	CH_3	2.12 d (5.0)	3.03 d (5.0)[b]	6.3—7.8 m	6.3—7.8 m	6.3—7.8 m	8.72 d (7.7)

[a] s = singlet, d = doublet, q = quartet, m = multiplet, ( ) = splittings in c/s.
[b] additional uncompletely resolved splittings into a 1:2:1 triplet due to long-range couplings to the 4-hydrogens.
[c] additional uncompletely resolved splitting into doublet due to long-range coupling to the 4-hydrogen.
[d] broad multiplet.

in the 4-positions. Similar couplings are often observed in methylthiophenes [26,27] and their sign has been determined,[28,29] It is, however, of interest to note that in 3-methylthiophenes the small couplings to the 4- and 5-hydrogens are of the same magnitude.

In the NMR-spectrum of the phenylsubstituted derivatives (XV, XXIV; R = C_6H_5) the CH—CH_2 groupings of the carbocyclic ring give ABX pattern. The geminal coupling is 17.4 c/s and 18.8 c/s, which are of the same magnitude as those observed in indanones,[30,31] This could indicate that the angle is somewhat smaller than the tetrahedral angle.[32] A large geminal coupling constant was also observed in cyclopenten-3,5-dione.[32] The magnitude of the two vicinal couplings deviates appreciably from those observed in 1,2-substituted indanes.[31] Although it seems quite unsafe to apply the Karplus equation [33] for a detailed conformational analysis of the ring-system due to the presence of electronegative substituents,[34] it can be noticed that the coupling constants do not deviate very much from those expected for a planar ring. In such a system the dihedral angles are 0° and 120°, leading to 8.0 c/s and 4.0 c/s, respectively. In the unsubstituted and methyl substituted thiaindanones the carbocyclic ring-hydrogen resonances give rise to a complex pattern due to additional couplings.

The NMR-spectrum of 5,6-dihydro-5-methyl-4H-cyclopenta[b]thiophene-4-one is similar to that of the above mentioned ketones. The thiophenic hydrogen resonances occur as doublets (5.1 c/s) at 2.67 τ and 2.92 τ. The lower field resonance is, on chemical shift consideration, assigned to hydrogen 3. This assignment is confirmed by the additional incompletely resolved long range coupling in the low field doublet. Studies of substituted 2-methylthiophenes have shown that the methyl group has a larger coupling to the 4- than the 5-hydrogen.[25] The methyl group resonance occurs at 8.72 τ as a doublet (7.7 c/s), while the CH—CH_2 group occurs as a complex band between 6.25—7.75 τ.

EXPERIMENTAL

Acylation of thiophenes. (a) 2-Acetyl and 2-propionylthiophene were prepared by acylation of thiophene with the respective anhydride according to the literature method.[35] 3-Propionyl-2,5-dimethylthiophene was prepared by acylation of 2,5-dimethylthiophene with propionic anhydride, using boron trifluoride etherate as catalyst according to Farrar and Levine.[36] 3-Propionylthiophene was prepared by treatment of 3-thienyllithium with propionaldehyde and oxidation of the alcohol with chromic acid according to Gronowitz.[20]

(b) *Benzyl-(2-thienyl)ketone.* A mixture of 60 g of thiophene (0.715 mole) and 80 g of phenylacetic acid (0.59 mole) in 50 ml of methylene chloride was added with stirring over 10 min to 200 g of PPA at 55° and the mixture stirred at this temperature for a further 1 h, when most of the methylene chloride distilled off. The red product was then poured into water and the resulting yellow oil, extracted with ether, and the solution dried and fractionated under vacuum. The colourless fraction, b.p. 187—91°/13 mm, (n_D^{19} = 1.6148) solidified and the solid (85 g, 71.5 %) crystallised as white needles from petroleum ether (b.p. 50—70°), m.p. 50—51°. (Found: C 71.25; H 4.84; S 15.69. Calc. for $C_{12}H_{10}OS$ (202.3): C 71.24; H 4.99; S 15.86). (Lit. [37] m.p. 51° from 50 % ethanol).

2,4-Dinitrophenylhydrazone. M.p. 182.5—184°. (Found: C 56.58; H 3.76; S 8.37. Calc. for $C_{18}H_{14}N_4O_4S$ (382.4): C 56.52; H 3.69; S 8.39). (Lit. [37] m.p. 180°).

(c) *2-Crotonylthiophene.* A mixture of 17.3 g (0.21 mole) crotonic acid and 20 g (0.238 mole) of thiophene in 50 ml of methylene chloride was added to PPA at 35° over 1 h with stirring. After 40 min additional stirring at this temperature the product was worked up

as above to give 13.4 g of 2-crotonylthiophene (44 %), b.p. 127–9°/12 mm, n_D^{23} 1.5949. (Lit.[38] b.p. 134.5–135.5°/14 mm, n_D^{25} = 1.5949). NMR: (CCl_4) τ_3 = 1.93 ppm, τ_5 = 2.38 ppm, τ_4 = 2.90 ppm, J_{35} = 1.2 c/s, J_{34} = 3.8 c/s, J_{45} = 5.2 c/s, CH=CH-band centered at τ = 3.10 ppm, τ_{CH_3} = 8.08 ppm, $J_{CH_3\text{-}CH}$ = 5.4 c/s.

(d) *4,5-Dihydro-5-methyl-6H-cyclopenta[b]thiophene-6-one.* When 50 g (0.595 mole) of thiophene and 61.5 g (0.715 mole) of methacrylic acid in 50 ml of methylene chloride were added to PPA at 55° with stirring over 30 min and the solution stirred an extra 1 h and worked up as before, 36 g (40 %) of the title compound was obtained, b.p. 137–40°/15 mm, n_D^{25} = 1.5812. (Lit.[8,10] b.p. 106°/2 mm, n_D^{20} 1.5808).

(e) *2-(β,β-Dimethylacryloyl)-thiophene.* When 16.8 g (0.2 mole) of thiophene and 9.4 g (0.094 mole) of β,β-dimethylacrylic acid were added in 20 ml of methylene chloride solution to stirred PPA at 35° over 10 min and stirred for an extra 25 min at 35°, 9.4 g (60.5 %) of the title product was obtained in the above manner, b.p. 132–7°/13 mm, n_D^{23} = 1.5913. (Found: C 64.97; H 5.95; S 19.65. Calc. for $C_{19}H_{10}OS$ (166.2): C 65.00; H 6.07 S 19.30).

2,4-Dinitrophenylhydrazone. M.p. 137°. (Found: C 51.85; H 4.24; S 9.10. Calc. for $C_{15}H_{14}N_4O_4S$ (346.3): C 52.00; H 4.08; S 9.26).

(f) *2-Cinnamoyl thiophene.* When 10 g (0.119 mole) of thiophene and 14.8 g (0.1 mole) of cinnamic acid in 15 ml of methylene chloride were treated with PPA as in (e), the title product was obtained as a solid (16.8 g, 79 %) which crystallised as white plates from ligroin, m.p. 81–2° (lit.[39] 80°).

(g) When 2,5-dimethylthiophene was treated with methacrylic acid under a variety of conditions only a high boiling, viscous, non-ketonic product was obtained and was not further examined.

Synthesis of Mannich bases. (a) *From 2-propionylthiophene.* A mixture of 140 g (1 mole) of 2-propionylthiophene, 36 g (1.2 mole) of paraformaldehyde, 98 g (1.2 mole) of dimethylamine hydrochloride, 5 ml of conc. hydrochloric acid and 120 ml of 95 % ethanol was refluxed for 15 h, the ethanol removed under vacuum and water added (500 ml). A small amount of oil was extracted with ether and the ether extract discarded. The aqueous phase was made alkaline with ammonium hydroxide and extracted three times with ether. The combined ether extracts were washed with water, dried ($MgSO_4$) and dry hydrogen chloride passed into the solution. The white precipitate of the Mannich base weighed 216 g (95 %) after drying. Crystallisation from ethanol gave 3-dimethylamino-2-methyl-1-(2-thienyl)-propanone hydrochloride as white needles, m.p. 154–6°. Burckhalter and Sam [10] record m.p. 154–6°.

(b) In a similar way we obtained the Mannich base hydrochlorides: from *2-acetylthiophene*, 3-dimethylamino-1-(2-thienyl)-propanone hydrochloride (89 %, m.p. 178–180° (lit.[10] 178–9°)), from 3-propionylthiophene, 3-dimethylamino-1-(3-thienyl)-propanone hydrochloride [88 %, white needles from acetone, m.p. 168–9° (Found: C 51.19; H 6.92; S 13.68. Calc. for $C_{10}H_{16}ClNOS$ (233.8): C 51.38; H 6.90; S 13.72)], from *2-phenylacetylthiophene*, the free Mannich base 3-dimethylamino-2-phenyl-1-(2-thienyl)-propanone [87 %, white needles from petroleum ether (b.p. 80–100°), m.p. 110°. (Found: C 69.65; H 6.64; S 12.44. Calc. for $C_{15}H_{17}NOS$ (259.4): C 69.50; H 6.61; S 12.37). [9 % starting material recovered from first ether extract], *from 2,5-dimethyl-3-propionylthiophene*, 3-dimethylamino-2-methyl-1-(2,5-dimethyl-3-thienyl)-propanone hydrochloride (83 %). (Found: C 55.26; H 7.64; S 12.64. Calc. for $C_{12}H_{20}ClNOS$ (261.7): C 55.10; H 7.65; S 12.26).

Decomposition of the Mannich bases. (a) The Mannich base hydrochloride and 0.2 g of hydroquinone were heated in an oil bath at 200° with a nitrogen bleed at 0.15 mm for 10–15 min, the product in most cases being distilled off. The product was washed with water, dried and redistilled. In this way the following compounds were obtained: *2-methacryloylthiophene* (79 %, b.p. 112–3°/17 mm (lit.[10] 118–20°/19 mm)), *3-methacryloylthiophene* [65 %, 110–14°/14 mm, n_D^{20} = 1.5672. (Found: C 63.12, H 5.48. Calc. for C_8H_8OS (152.2): C 63.18; H 5.30)], *α-styryl-2-thienylketone* (81 %, product did not distil but was isolated by adding water to the residue and extracting with chloroform. The dried ($MgSO_4$) chloroform extract on evaporation gave a yellow solid which crystallised as pale yellow rhombs from ethyl acetate/ligroin, m.p. 142.5–143.5°. (Found: C 72.73; H 4.68; S 15.23. Calc. for $C_{13}H_{10}OS$ (214.3): C 72.90; H 4.71; S 14.98). *2-acryloylthiophene* (51 %, product became viscous on standing, b.p. 113–7°/14 mm (lit. [10] b.p. 108–10°/12 mm), *2,5-dimethyl-3-methacryloylthiophene* [69 %, b.p. 107–9°/9 mm, n_D^{25} =

1.5437. (Found: C 66.71; H 6.81; S 17.54. Calc. for $C_{10}H_{12}OS$ (180.3): C 66.60; H 6.71; S 17.80)].

Cyclisation of unsaturated ketones. (a) *4,5-Dihydro-5-methyl-6H-cyclopenta[b]thiophene-6-one.* 2-Methacryloylthiophene (30 g) was added dropwise to PPA (100 g) at 50° and the mixture stirred for 1 h. The solution was diluted with water, ether extracted and the dried ($MgSO_4$) extract fractionated. The product (25.3 g, 84 %), b.p. 115-9°/7 mm, was identical with that previously reported.

(b) *5,6-Dihydro-5-methyl-4H-cyclopenta[b]thiophene-4-one.* When 22.5 g of 3-methacryloylthiophene was treated as above, the title compound (17.3 g, 77 %) was obtained, b.p. 115-9°/9 mm (lit.[8] 88—98°/0.7 mm).

(c) *4,5-Dihydro-4-methyl-6H-cyclopenta[b]thiophene-6-one.* When 2-crotonylthiophene (10 g) was treated as above for 4 h at 100° and the product worked up as before, 6.8 g (68 %) of the cyclic ketone were obtained, b.p. 130—132°/12 mm, n_D^{20} = 1.5809. (Found: C 63.15; H 5.12, S 21.03. Calc. for C_8H_8OS (152.2): C 63.18; H 5.30; S 21.08).

2,4-Dinitrophenylhydrazone, m.p. 197—202°. (Found: C 50.28; H 3.48; S 9.76. Calc. for $C_{14}H_{12}N_4O_4S$ (332.3): C 50.57; H 3.64; S 9.65).

(d) *4,5-Dihydro-4,4-dimethyl-6H-cyclopenta[b]thiophene-6-one.* When 14 g of 2-(β,β-dimethylacryloyl)thiophene was treated as in (c), 9.6 g (69 %) of the title product was obtained, b.p. 120—3°/11 mm. (Found: C 65.04; H 6.13; S 18.96. Calc. for $C_9H_{10}OS$ (166.2): C 65.03; H 6.07; S 19.3).

(e) *4,5-Dihydro-4-phenyl-6H-cyclopenta[b]thiophene-6-one.* Treatment of 1.2 g of 2-cinnamoylthiophene with PPA for 4 h at 100° followed by the above work up procedure gave 0.9 g (75 %) of the indanone analogue as a pale brown solid. Recrystallisation from petroleum ether (b.p. 50—70°) gave the product as white needles, m.p. 84.5—85°.(Found: C 73.15; H 4.75; S 14.95. Calc. for $C_{13}H_{10}OS$ (214.3): C 72.88; H 4.71; S 14.98).

2,4-Dinitrophenylhydrazone, m.p. 175—8°. (Found: C 57.56; H 3.58; S 7.90. Calc. for $C_{19}H_{14}N_4O_4S$: C 57.81; H 3.75; S 8.13).

(f) *4,5-Dihydro-5-phenyl-6H-cyclopenta[b]thiophene-6-one.* When α-phenylacryloylthiophene (5 g) was treated under various conditions of temperature and solvent with PPA only very low yields of product were isolated. Under the conditions of (c) 0.15 g (3 %) of the cyclic ketone was isolated, m.p. 96° (lit.[8] gives 96—7°).

(g) When 2-acryloyl or 2,5-dimethyl-3-methacryloylthiophene were treated under various conditions only polymeric and tarry material was isolated.

2,5-Dibromo-3-methylthiophene. A mixture of 20 g (0.2 mole) of 3-methylthiophene in 100 ml of acetic acid was treated dropwise over 1/2 h with 68 g (23.3 ml, 0.41 mole) of bromine in 50 ml of acetic acid with cold water cooling and stirring. After a further 2 h stirring the product was poured onto ice, neutralised with sodium hydroxide and ether extracted. The dried extract was fractionated to give 45.8 g (88 %) of the product, b.p. 130—2°/45 mm (Steinkopf and Jacob [40] give 226—30°/760 mm).

2,5-Dibromo-3-bromomethylthiophene. A mixture of 43.3 g (0.169 mole) of 2,5-dibromo-3-methylthiophene, 30.1 g (0.169 mole) of N-bromosuccinimide, 100 ml of carbon tetrachloride, 0.5 g of benzoyl peroxide and 4 drops of water was refluxed with stirring for 2 h. The mixture was filtered, the residue washed well with carbon tetrachloride and the filtrate evaporated under vacuum to leave 56.6 g (100 %) of an orange oil. The product was used directly in the next step.

β-(2,5-Dibromo-3-thienyl)propionic acid. To 3.9 g (0.17 mole) of sodium dissolved in 150 ml of absolute alcohol was added 27.1 g (0.17 mole) of diethyl malonate. To the refluxing solution was added dropwise 56.5 g (0.169 mole) of the above oil and the resulting solution refluxed a further 6 h with precipitation of 11.8 g of sodium bromide. Most of the ethanol was evaporated and then water added and the mixture extracted with ether. The dried ($MgSO_4$) extract was fractionated to give 26 g (40 %) of diethyl-(2,5-dibromo-3-thienyl)malonate, b.p. 144—51°/0.8 mm. 19.0 g of a higher boiling fraction (b.p. 200—240°/0.8 mm) was also obtained which solidified and crystallised as white prisms from ligroin, m.p. 66°. This was *diethyl bis(2,5-dibromo-3-thienyl)-malonate.* (Found: C 30.68; H 2.54; Br 47.86; S 9.71. Calc. for $C_{17}H_{16}Br_4O_4S_2$ (668.1): C 30.57; H 2.41; Br 47.90; S 9.60). Hydrolysis of the lower boiling product with ethanolic potassium hydroxide for 6 h under nitrogen, followed by removal of the ethanol addition of water and acidification, gave an oily solid which eliminated carbon dioxide when heated at 130° for 1 h. The decarboxylated residue gave 10.3 g of *β-(2,5-dibromo-3-thienyl)-propionic acid* as white prisms from ligroin, m.p. 89°. (Found: C 26.80; H 1.73; S 10.09. Calc. for $C_7H_6BrO_2S$

(234.1): C 26.76; H 1.93; S 10.21). In a similar hydrolysis the higher boiling fraction gave *bis(2,5-dibromo-3-thienyl)acetic acid*, m.p. 144°, as white needles from ethanol. (Found: C 25.73; H 1.47; S 11.53. Calc. for $C_{12}H_6Br_4O_2S_2$ (568.0): C 25.36; H 1.42; S 11.29).

2-Bromo-4,5-dihydro-6H-cyclopenta[b]thiophene-6-one. When 2 g of β-(2,5-dibromo-3-thienyl)propionic acid was stirred with 20 g of PPA at 80° for 1 h and the product worked up in the usual way, 0.7 g of the title compound was obtained and crystallised as rods from ligroin, m.p. 116°. (Found: C 38.96; H 2.37; Br 36.42. Calc. for C_7H_5BrOS (217.1): C 38.73; H 2.32; Br 36.80).

2,4-Dinitrophenylhydrazone. M.p. 263°. (Found: C 39.80; H 2.39; S 7.67. Calc. for $C_{13}H_9BrN_4O_4S$ (397.2): C 39.34; H 2.28; S 8.08).

3-Thenoic anhydride. To a suspension of 6.9 g (0.054 mole) of 3-thenoic acid in water was added sodium hydroxide solution until the solution was neutral to phenolphthalein. To the rapidly stirred (magnetic stirrer used) solution were added 2 drops of pyridine and then (dropwise) 7.9 g (0.054 mole) of 3-thenoyl chloride in 10 ml of acetone. After 15 min stirring the product was filtered off and washed with cold water and then a little petroleum ether (b.p. 40—60°). The product was dried in a desiccator to give 11.6 g (90 %) of 3-thenoic anhydride, m.p. 53—6° (lit.[41] gives 54.5—56°).

2-Cyclohexylthiophene-4-carboxylic acid. A mixture of 9.5 g (0.04 mole) of 3-thenoic anhydride and 6.56 g (0.08 mole) of cyclohexene was added dropwise to 100 g of PPA at 57° during 5 min. Stirring at this temperature was continued for a further 25 min after which the mixture was poured into water and extracted three times with ether. The ether extract was washed thoroughly with sodium bicarbonate solution and dried ($MgSO_4$) and evaporated. The residue (5.1 g) was not ketonic and did not contain sulphur and distilled to give a colourless liquid, b.p. 90—100°/7.5 mm, $n_D^{21.5} = 1.4877$. From the bicarbonate washings by acidification was obtained 3.3 g of 2-cyclohexylthiophene-4-carboxylic acid (39 %) which recrystallised from aqueous ethanol as white needles, m.p. 176°. (Found: C 62.65; H 6.64; S 14.89. Calc. for $C_{11}H_{14}O_2S$ (210.3): C 62.80; H 6.71; S 15.25). NMR: (acetone) τ_5 1.99 ppm; τ_3 2.75 ppm, $J_{35} = 1.5$ c/s; $J_{3\text{-}CH} = 1.5$ c/s.

β-(2-Acetyl-3-thienyl)-propionic acid. Treatment of 1 g of β-(3-thienyl)-propionic acid in 10 ml of acetic acid with 25 g of PPA at room temperature for 1/2 h followed by the usual work-up gave the title compound (0.85 g) as white crystals from petroleum ether (b.p. 100—140°), m.p. 114—6°. (Found: C 54.79; H 5.02. Calc. for $C_9H_{10}O_3S$: C 54.53; H 5.09). NMR: ($DCCl_3$) τ_5 2.54 ppm, τ_4 2.92 ppm, $J_{45} = 5.0$ c/s.

The NMR-spectra were obtained on a Varian A-60 NMR spectrometer and the IR-spectra were recorded on a Beckman IR-5A infrared spectrophotometer.

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