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CYCLISATIONS WITH METHACRYLIC ACID IN PPA. ON THE SYNTHESIS OF CYCLOPENTA[b]THIOPHENONES

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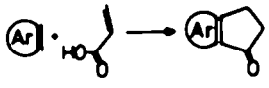
Abstract—The reaction between some 2-substituted thiophen derivatives and methacrylic acid in PPA has been studied. Isomeric cyclopenta[b]thiophen ketones were formed in several cases, depending on the substituents. Features of their ^{13}C and ^{1}H NMR spectra are discussed and evidence is presented for ring-closure of 3(2-thienyl)propionic acids without rearrangement, in contrast to statements in the literature.

The acid promoted cyclisation of α,β-unsaturated acids and aromatic compounds to give cyclopenta-annellated aromatic derivatives (indanone analogues) should be an attractive route to such systems, but has been the subject of only a few investigations.[1-4]



Since we were interested in preparing substituted cyclopenta[b]thiophen derivatives as substrates in ring-opening reactions,[5] we treated different thiophen derivatives with methacrylic acid in PPA, essentially as described by Meth-Cohn and Gronowitz.[3]

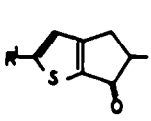
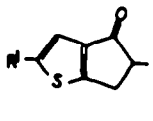
RESULTS

A mixture of methacrylic acid and the thiophen derivative (1:1) in methylene chloride was added to PPA (excess) at 50–60°. We found that two isomers, 1 and 2, were formed from thiophen, 2-methyl, 2-t-butyl- and 2-phenylthiophen (Table 1). This formation of isomers has not been observed in other systems. On the contrary, it is stated that only one isomer is produced in the reactions between methyl substituted anisoles and methacrylic acid in PPA.[4]

On closer examination of the higher boiling fraction of the methacrylic acid cyclisation with 2-chlorothiophen, we found that the main product was the ketone 3(R = Cl, 26% isolated yield) and with 2-methylthiophen, the ketone 3(R = Me, 4%) was formed to a smaller extent. With 2-phenylthiophen, two compounds with mass number 388 were formed, which could be isomers of 3(R = Ph).

Considerable amounts of polymers were formed in all of the cyclisation experiments, and we were able to show that a catalytic amount of methacrylic acid in PPA polymerized 2-methylthiophen to the extent of 85% at 50–60° during 1 hr. An experiment without the methacrylic acid left 85% of the methylthiophen intact under the same conditions. We also isolated a high boiling fraction consisting of two different trimers[7] of 2-methylthiophen from one of the ordinary cyclisation experiments with 2-methylthiophen, methacrylic acid and PPA. Thus this direct cyclisation reaction is of limited value unless the polymerisation reactions can be suppressed. However,

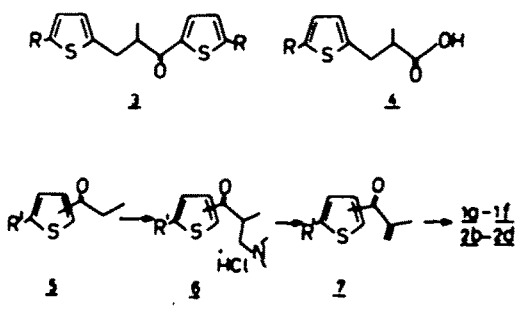
Table 1. Yields and ratios of cyclised products in the reaction between 2-substituted thiophen derivatives and methacrylic acid in PPA

Ratios[a] and yields[b] of cyclised products 1 and 2	R^1		
99:1 (7%)[c]	H	1a	2a
70:30 (15%)	Me	1b	2b
90:10 (40%)	tBu	1c	2c
60:40 (15%)	Ph	1d	2d
100:0 (17%)	Cl	1e	
100:0 (6%)	SMe	1f	

[a]Determined by GC. [b]Isolated yields after distillation or recrystallisation. [c]The yield of 1a was reported to be 40% in Ref. 3, which we were not able to reproduce.

since it is a one step route to the bicyclic systems it may be useful in selected cases, e.g. the t-butyl case (Table 1).

All of the compounds **1a–1f** were independently synthesized by known routes[3,9] via the 2-propionylthiophenes **5** followed by the Mannich reaction and thermal elimination of the hydrogen chloride salts **6** to give the α,β-unsaturated ketones **7**, which were finally cyclized with PPA. Also **2b–2d** were prepared via this route, starting from the 3-propionylthiophenes **5** (Scheme 1).



Scheme 1.

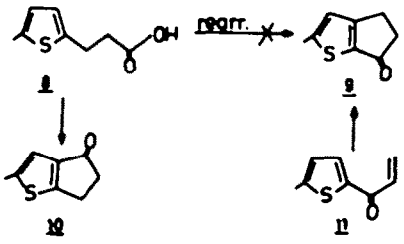
DISCUSSION

The 6-ones (**1**) are most likely formed by Friedel-Crafts acylation of the thiophen nucleus to give α,β-unsaturated cetones **7** (the 2-isomers), which subsequently cyclize. In fact the ketones **7** (the 2-isomers) were observed in the reaction mixtures at early stages of the reactions and **7** are easily cyclized with PPA, as mentioned above. The α,β-unsaturated ketones **7** gave the cyclic ketones **1a–1f** and **2b–2d** respectively, without traces of rearrangement. (For structural assignments *vide infra*.) This observation is important, since an acylation has recently been shown to be reversible in PPA.[10]

The 4-ones (**2**) are probably formed via the thienylpropionic acids **4** followed by cyclisation. This is indicated by the presence of small amounts of **4**(R = Me) in the mixture with 2-methylthiophen and methacrylic acid in PPA (detected as its trimethylsilyl ester), and also by a control experiment in which **4**(R = Me) was treated with PPA in the presence of methacrylic acid. In this way, **2b** was formed in about 30% yield. If the methacrylic acid was omitted the cyclisation did not take place to more than 1% under otherwise identical conditions. This is in agreement with the results of Sam and Thompson,[6] who reported a 0% yield in ring closure attempts with 2-methyl-3-(2-thienyl)propionic acid with PPA at 30–80° for 0.25–12 hr. The action of methacrylic acid is obscure, but a change of the acidity of the medium may be part of an explanation.

The relative proportions of **1** and **2** do not reflect the ratio of acylation vs alkylation. First of all the yields are too low and also the initially formed acylated intermediates **7** (2-isomers) are partially consumed in competitive reactions, e.g. to give the ketones of type **3**.[11,2b]

During the course of this work, Palmer *et al.*[8] reported that 3-(2-methyl-5-thienyl)propionic acid (**8**) rearranged completely in PPA at 100° to give the 6-one derivative **9** exclusively (Scheme 2). Obviously, the same kind of



Scheme 2.

rearrangement could also be responsible for the formation of the 6-ones in our cases. We therefore repeated the experiment of Palmer *et al.* and isolated a compound with the same m.p. and NMR (^{1}H and ^{13}C) data as Palmer *et al.* reported (Table 2). Since we had the ^{1}H and ^{13}C data of several similar compounds (the ketones **1** and **2**) it seemed more likely to us that the compound we and Palmer *et al.* had isolated was the 4-one derivative **10**. The chemical shift of 3-C consistently appears at higher field (5–6 ppm) for the 4-ones than for the 6-ones (Table 2).

We also prepared the 6-one **9** by an independent route (from **11** and PPA) and could show that this ketone had the ^{13}C shifts consistent with the other 6-ones, and also had a different retention time on GC (co-injection), different m.p. and different polarity on tlc than the 4-one **10**. (The 4-ones are less polar than the 6-ones.) In order to exclude the somewhat unlikely situation that all ring-closures described in this paper occur with complete rearrangement, the dipole moments of **1e** and **2e** were determined in benzene and found to be 4.6 ± 0.1 D and 3.5 ±

Table 2. ^{1}H and ^{13}C chemical shifts for 3-H and 3-C of the 4- and 6-ones in $CDCl_3$ relative to TMS

6-ones	$\delta_{3\text{-H}}$	$\delta_{3\text{-C}}$	$\delta_{3\text{-C}}$	$\delta_{3\text{-H}}$	4-ones
1a	7.09	123.9	119.6	7.10	2a
1b	6.73	122.6	116.9	6.77	2b
	6.82[a]			6.75[a]	
1c	6.83	118.8	113.0	6.88	2c
1d	7.20	119.7	114.6	7.31	2d
1e	6.99	123.8			
9	6.74	122.6	116.7	6.76	10

a) In acetone-d_6

0.1 D respectively, which agree with the expected polarities of these substances and lend support to our structural assignments.[12] Thus, the 3-(2-thienyl)propionic acids *do not* rearrange under these conditions (PPA, 50–100°).

From the paper by Palmer *et al.*[8] one gets the impression that **9** and **10** have identical ^{1}H NMR spectra. The major difference, however, is the pattern of the CH_2 resonances. While in **9** the two CH_2 resonances are indistinguishable (appearing as an irregular multi-line band centered at 2.90 δ) they are clearly separated in **10** (as Palmer *et al.* reported for **9**); a broad three line band at 3.06–3.16 δ (centered at 3.11 δ) and a sharp 10 line band at 2.81–2.93 δ (centered at 2.87 δ).

Furthermore the 3-protons of the 6-ones and the 4-ones have very similar chemical shifts. The differences are in some cases less than 0.05 ppm and the shifts are solvent dependent (Table 2). Thus the diagnostic value of the ^{1}H resonance spectra of these compounds is limited.

The assignment of the low field (7.33 δ) resonance of 5,6 - dihydro - 5 - methyl - 4H - cyclopenta[b]thiophen - 4 - one (**2a**) to 3-H by Meth-Cohn and Gronowitz[3] may be called to question based on our findings that the 3-H resonance of **2b** appears at 6.77 δ. The only difference between **2a** and **2b** is the presence of a Me group in the 2-position of **2b**, which should shift the 3-H resonance 0.37 ppm to higher field compared to a hydrogen.[13]

With the assignment in Ref. 3, the difference in these two cases is 0.56 ppm, which we feel is too large. However, the difference between the high field aromatic resonance (7.08 δ) of **2a** and that of 3-H of **2b** is of the right order of magnitude, i.e. 0.31 ppm. We therefore suggest that the *high* field part (7.08 δ) of the aromatic resonances of **2a** be assigned to 3-H.

Moreover, since the 3-H signal of the 2-substituted bicyclic ketones is little affected by the orientation of the cyclopenta[b]ketone moiety (Table 2), one would expect the 3-H signal of **1a** and **2a** also to be essentially unaffected, which is the case for their high field aromatic signals. Their low field aromatic signals appear at 7.97 for **1a** and at 7.33 for **2a**. This difference (0.64 ppm) is considerably larger than expected, compared with 2- and 3-acetylthiophen (difference 0.30 ppm). The rigidity of the bicyclic ketones may be responsible for both a stronger electron withdrawing effect on the 2-proton of **1a** and a stronger anisotropy effect operating on the 3-proton of **2a**, thus counteracting the electron withdrawing effect in this latter case. Long-range couplings (0.4–0.5 Hz splittings) between 3-H and 4-CH_2 were observed for the 6-ones **1a**, **1b**, **1c**, **1e** and **1f**,[14] but long-range couplings between 3-H and 6-CH_2 of the 4-ones **2a**, **2b** and **2c** were not visible.

EXPERIMENTAL

The PPA was Merck's commercial quality, THF and diethylether were dried and distilled over Na with benzophenone as indicator, and commercial CH_2Cl_2 was purified by passage through a basic alumina column. ^{1}H NMR spectra were recorded with a Joel MH 100 and a Varian A 60 spectrometer. The ^{13}C NMR spectra were recorded with a Jeol FX-60 NMR spectrometer. M.ps and b.ps are uncorrected. IR spectra were recorded with a Perkin–Elmer 257 IR Grating spectrometer. Gas chromatograms were recorded with a Perkin–Elmer 900 Gas Chromatograph equipped with a Varian 481 Digital Integrator. Dipole moments were determined with a WTW type DM 01 dipole meter.

General description of the direct cyclisations with methacrylic acid, PPA and thiophen derivatives (essentially as given in Ref. 3). The 2-substituted thiophen derivatives together with 1.2 eq of methacrylic acid in an equal volume of CH_2Cl_2 were added dropwise to PPA (5.0 g per mmol of the thiophen derivative) at 50–60° during 30 min. The mixtures were stirred for 1 hr at this temp., cooled, hydrolyzed with ice-water and extracted with ether. The ethereal phases were dried ($MgSO_4$), evaporated and distilled or recrystallised to give the products shown in Table 1. GC traces were recorded on the crude ethereal extracts (3% OV 1, Chromosorb Q 80/100, 70–300°, 12°/min) and the isomer distribution determined after comparison of retention times with authentic materials and of mass spectra. The ^{13}C NMR spectra of the purified reaction products were also compared with those of authentic materials.

Syntheses of authentic cyclopenta[b]thiophen ketones

4,5-Dihydro-2,5-dimethyl-6H-cyclopenta[b]thiophen-6-one (**1b**). To 100 g of PPA, 4.4 g (0.023 mol) of 5-methyl-2-methacryloylthiophen was added dropwise at 50°. Stirring was continued for 1 hr and then the mixture was hydrolysed with ice-water, extracted with ether, washed with $NaHCO_3$ aq, dried and evaporated. Distillation afforded **1b** in 82% yield, b.p.$_{0.1}$ 81–82°. IR(NaCl) 1700 cm^{-1} C=O. NMR(acetone-d_6): 1.22(d, 3H, 5-CH_3), 2.55 (d, 3H, 2-CH_3), 2.31–3.42 (m, 3H, CH_2, CH), 6.82 (m, 1H, 3-H). $J_{3\text{-}H,2\text{-}CH_3}$ 1 Hz, $J_{CH,5\text{-}CH_3}$ 7 Hz. (Found: C, 64.96; H, 6.03; S, 19.38. $C_9H_{10}OS$ requires: C, 65.03; H, 6.06; S, 19.29%). In a similar way we obtained the following ketones.

4,5-Dihydro-2-t-butyl-5-methyl-6H-cyclopenta[b]thiophhen-6-one (**1c**), yield: 54% from 5-t-butyl-2-methacryloylthiophen, b.p.$_1$ 124–126°, n_D^{22} 1.5507, d^{22} 1.084, R_D 61.3 ml/mol, μ 4.6 ± 0.1 D. IR(NaCl) 1695 cm^{-1} C=O. NMR($CDCl_3$): 1.31(d, 3H, 5-CH_3), 1.41(s, 9H, tBu), 2.54(q, 1H, 4-H *trans*), 3.18(q, 1H, 4-H *cis*), 2.93(10 lines, 1H, 5-H), 6.83(bs, 1H, 3-H). $J_{4\text{-}H_{trans},4\text{-}H_{cis}}$ 17 Hz, $J_{4\text{-}H_{cis},5\text{-}H}$ 6.8 Hz, $J_{4\text{-}H_{trans},5\text{-}H}$ 2.5 Hz, $J_{5\text{-}CH_3,5\text{-}H}$ (6.3 Hz. (Found: C, 68.7; H, 7.79. $C_{12}H_{16}OS$ requires: C, 69.2; H, 7.74%).

4,5-Dihydro-2-phenyl-5-methyl-6H-cyclopenta[b]thiopen-6-one (**1d**), yield: 18% from 2-methacryloyl-5-phenylthiophen, m.p. 111–112° (hexane). IR(KBr): 1680 cm^{-1} C=O. NMR($CDCl_3$): 1.34(d, 3H, 5-CH_3), 2.59(q, 1H, 4-H *trans*), 3.26(q, 1H, 4-H *cis*), 2.98(10 lines, 1H, 5-H), 7.20(s, 1H, 3-H), 7.3–7.6(m, 5H, C_6H_5). $J_{4\text{-}H_{trans},4\text{-}H_{cis}}$ 16.7 Hz, $J_{4\text{-}H_{cis},5\text{-}H}$ 6.7 Hz, $J_{4\text{-}H_{trans},5\text{-}H}$ 2.4 Hz, $J_{5\text{-}CH_3,5\text{-}H}$ 7.4 Hz.

4,5-Dihydro-2-phenyl-5-methyl-6H-cyclopenta [b] thiophen-6-one (**1e**), yield: 68% from 2-chloro-5-methacryloylthiophen[6] (reaction temp. 80°), b.p.$_{0.5}$ 103–105°, n_D^{25} 1.5926. IR(NaCl): 1700 cm^{-1} C=O, (lit.[6] b.p.$_{0.8}$ 91°, n_D^{25} 1.5887). NMR ($CDCl_3$): 1.32(d, 3H, 5-CH_3), 2.58(dq, 1H, 4-H *trans*), 3.28(dq, 1H, 4-H *cis*), 2.92(10 lines, 1H, 5-H), 6.99(t, 1H, 3-H). $J_{3\text{-}H,4\text{-}H}$ 0.4 Hz, $J_{4\text{-}H_{trans},4\text{-}H_{cis}}$ 17.0 Hz, $J_{4\text{-}H_{trans},5\text{-}H}$ 6.7 Hz, $J_{4\text{-}H_{trans},5\text{-}H}$ 2.6 Hz, $J_{5\text{-}H,5\text{-}CH_3}$ 7.3 Hz. (Found: C, 51.5; H, 3.74. C_8H_7ClOS requires: C, 51.48; H, 3.78%).

4,5-Dihydro-2-methylthio-5-methyl-6H-cyclopenta[b]thiophen-6-one (**1f**), yield: 20% from 2-methylthio-5-methacryloylthiophen, b.p.$_{0.8}$ 127–130°. IR(NaCl): 1690 cm^{-1} C=O. NMR($CDCl_3$): 1.28(d, 3H, 5-CH_3), 2.58(s, 3H, SCH_3), 2.54(q, 1H, 4-H *trans*), 3.22(q, 1H, 4-H *cis*), 2.93(10 lines, 1H, 5-H), 6.87(s, 1H, 3-H). $J_{4\text{-}H_{trans},4\text{-}H_{cis}}$ 17.0 Hz, $J_{4\text{-}H_{cis},5\text{-}H}$ 6.8 Hz, $J_{4\text{-}H_{trans},5\text{-}H}$ 2.3 Hz, $J_{5\text{-}CH_3,5\text{-}H}$ 7.3 Hz. (Found: C, 54.5; H, 5.22. $C_9H_{10}OS_2$ requires: C, 54.5; H, 5.08%).

5,6-Dihydro-2,5-dimethyl-4H-cyclopenta[b]thiophen-4-one (**2b**), yield: 61% from 2-methyl-4-methacryloylthiophen, b.p.$_{0.1}$ 81–83°. IR(NaCl): 1700 cm^{-1} C=O. NMR (acetone-d_6): 1.22(d, 3H, 5-CH_3), 2.47(d, 3H, 2-CH_3), 2.2–3.7(m, 3H, CH, CH_2), 6.73(m, 1H, 3-H). $J_{3\text{-}H,2\text{-}CH_3}$ 1.0 Hz, $J_{CH,5\text{-}CH_3}$ 6.5 Hz. (Found: C, 65.10; H, 6.10; S, 19.19. $C_9H_{10}OS$ requires: C, 65.03; H, 6.06; S, 19.29%).

5,6-Dihydro-2-t-butyl-5-methyl-4H-cyclopenta [b] thiophen-4-one (**2c**), yield: 50% from 2-t-butyl-4-methacryloylthiophen, b.p.$_{0.1}$ 95–96°, n_D^{22} 1.5429, d^{22} 1.086, R_D 60.5 ml/mol. μ 3.5 ± 0.1 D. IR(NaCl): 1705 cm^{-1} C=O. NMR($CDCl_3$): 1.28(d, 3H, 5-CH_3), 1.36(s, 9H, tBu), 2.72(q, 1H, 6-H *trans*), 3.40(q, 1H, 6-H *cis*), 2.92(m, 1H, 5-H), 6.89(s, 1H, 3-H). $J_{6\text{-}H_{cis},6\text{-}H_{trans}}$ 17.3 Hz, $J_{6\text{-}H_{cis},5\text{-}H}$ 6.7 Hz, $J_{6\text{-}H_{trans},5\text{-}H}$ 2.7 Hz, $J_{5\text{-}H,5\text{-}CH_3}$ 6.7 Hz. (Found: C, 68.9; H, 7.74; S, 15.5. $C_{12}H_{16}OS$ requires: C, 69.2; H, 7.74; S, 15.4%).

5,6-Dihydro-5-methyl-2-phenyl-4H-cyclopenta [b] thiophen-4-

one (2d), yield: 65% from 4-methacryloyl-2-phenylthiophen, m.p. 96–97° (hexane). IR(KBr): 1695 cm^{-1} C=O. NMR($CDCl_3$): 1.34(d, 3H, 5-CH_3), 2.74(q, 1H, 6-H *trans*), 3.43(q, 1H, 6-H *cis*), 2.98(10 lines, 1H, 5-H), 7.28–7.64(m, 6H, aromatic). $J_{6\text{-}H\,cis,6\text{-}H\,trans}$ 17.2 Hz, $J_{6\text{-}H\,cis,5\text{-}H}$ 6.6 Hz, $J_{6\text{-}H\,trans,5\text{-}H}$ 2.8 Hz, $J_{5\text{-}H,5\text{-}CH_3}$ 7.4 Hz. (Found: C, 73.8; H, 5.40. $C_{13}H_{12}OS$ requires: C, 73.7; H, 5.30%).

4,5-Dihydro-2-methyl-6H-cyclopenta[b]thiophen-6-one (9). A soln of 1.0 g (6.6 mmol) of 2-methyl-5-acryloylthiophen in 2 ml of CH_2Cl_2 was added to 30 g of PPA at 50°, whereupon the reaction temp. was gradually raised to 90° and kept there for 20 min. (At lower temp. the reaction was inconveniently slow.) The usual work-up gave 300 mg of crude 9, which was purified by prep tlc (2 mm silica, hexane/ethyl acetate 80/20), R_f 0.28–0.19, yield 240 mg, 24%. The substance crystallises on standing at room temp., m.p. 53–54°. IR(KBr): 1685 cm^{-1} C=O. NMR($CDCl_3$): 2.57(d, 3H, 2-CH_3), 2.90(m, 4H, CH_2) 6.74(m, 1H, 3-H). $J_{3\text{-}H,2\text{-}CH_3}$ 1.0 Hz. (Found: C, 63.09; H, 5.33. C_8H_8OS requires: C, 63.13; H, 5.30%).

5,6-Dihydro-2-methyl-4H-cyclopenta[b]thiophen-4-one (10). A mixture of 3-(5-methyl-2-thienyl)-propanoic acid and PPA was stirred at 100° for 3 hr and worked up (according to the description by Palmer *et al.*) to give a 30% yield of 10, m.p. 65–66° (petr. ether 60–70). (lit.[8] m.p. 65.5–66.5° for compound 9). IR(KBr) 1685 cm^{-1} C=O. NMR($CDCl_3$): 2.47 (pent, 3H, 2-CH_3), 2.81–2.93 (10 sharp lines, 2H, CH_2), 3.06–3.16 (3 broad lines, 2H, CH_2), 6.76(q, 1H, 3H). $J_{3\text{-}H,2\text{-}CH_3}$ 1.2 Hz.

Isolation of 2-methyl-di-1,3-(5-chloro-2-thienyl)-propan-1-one (3, R = Cl). This substance was obtained as a high boiling fraction from the product of 2-chlorothiophen and methacrylic acid in PPA. B.p.$_{1.5}$ 182–187°, yield 26%. NMR($CDCl_3$): 1.27(d, 3H, CH_3), 2.75–3.67(m, 3H, CH, CH_2), 6.60(q, 2H, β-protons of the 3-thienyl ring), 6.92(d, 1H, β-proton meta to the CO group of the 1-thienyl ring), 7.47(d, 1H, β-proton ortho to the CO group of the 1-thienyl ring). $J_{3,4\ thienyls}$ 3.5 Hz, $J_{CH_3,CH}$ 6.5 Hz. MS: Found : *m/e* 304 requires: 304 (for ^{35}Cl). IR(NaCl) 1660 cm^{-1} C=O. (Found: C, 47.7; H, 3.31; S, 20.66. $C_{12}H_{10}Cl_2OS_2$ requires: C, 47.22; H, 3.30; S, 21.0%).

Cyclisation of 2-methyl-3-(5-methyl-2-thienyl)-propanoic acid (4, R = Me). A mixture of 270 mg (1.47 mmol) of 4(R = Me), 1.35 g (15.7 mmol) of methacrylic acid and 150 mg (0.876 mmol) of dodecane (as internal standard) in 18 g of PPA was stirred at 50–55° for 1.5 hr. After hydrolysis and extraction with ether, a portion of the dried ($MgSO_4$) ethereal extract was silylated (Regisil) and analyzed with GC(OV 17, 3%, 1.7 m, 100–225°, 8°/min). The bicyclic ketone 2b was formed in 30-40% yield (three different experiments) and all of the starting material was consumed.

When this experiment was performed without methacrylic acid, only 1% of 2b was formed and 99% of the starting material was left unchanged.

2-Methyl-3-(5-methyl-2-thienyl)-propanoic acid (4, R = Me). To a soln of 2.7 g (0.12 mol) of Na in 154 ml of abs EtOH, 22.7 g (0.130 mol) of diethyl methyl malonate was added. After stirring for 1 hr, 17.4 g (0.119 mol) of 2 - methyl - 5 - thenylchloride was added dropwise and the mixture refluxed for 17 hr. A soln of 25.5 g (0.460 mol) of KOH in 25 ml of water was added to the EtOH soln and reflux continued for 24 hr. After evaporation of the EtOH the residue was treated with ice-water, neutralized with conc HCl and extracted with ether. Drying ($MgSO_4$), evaporation and distillation gave 5.9 g (25%) of the title compound, b.p.$_{0.3}$ 111–114°. IR(neat, NaCl): typical carboxylic acid and C=O at 1700 cm^{-1}. NMR($CDCl_3$): 1.22(d, 3H, 2-CH_3), 2.40(bs, 3H, 2Th-CH_3), 2.57–3.28(m, 3H, CH_2, CH), 6.57(bs, 2H, 3Th-H and 4Th-H), 11.85(s, 1H, COOH). (Found: C, 58.71; H, 6.55. $C_9H_{12}O_2S$ requires: C, 58.67; H, 6.56%).

The α,β-unsaturated ketones 7. The description given in Ref. 3 starting from the appropriate propionylthiophenes was followed.

2-Series

2 - Methacryloyl - 5 - methylthiophen (7, R' = Me). A 45% yield was obtained from 2 - propionyl - 5 - methylthiophen,[15] b.p.$_{0.15}$ 66–68°. NMR(acetone-d_6): 2.0(m, 3H, CH_3), 2.53(q, 3H, 5-CH_3), 5.75(m, 2H, =CH_2), 6.87(dq, 1H, 4-H), 7.55(dd, 1H, 3-H). $J_{3\text{-}H,4\text{-}H}$ 3.6 Hz, $J_{5\text{-}CH_3,4\text{-}H}$ 1.0 Hz, $J_{5\text{-}CH_3,3\text{-}H}$ 0.4 Hz. (Found: C, 64.97; H, 6.04; S, 19.18. $C_9H_{10}OS$ requires: C, 65.03; H, 6.06; S, 19.29%).

5-t-Butyl-2-methacryloylthiophen (7, R' = tBu), yield: 21% from 2-t-butyl - 5 - propionylthiophen,[16] b.p.$_{12}$ 146–148°. NMR($CDCl_3$): 1.40 (s, 9H, tBu), 2.04(m, 3H, CH_3), 5.70(m, 2H, =CH_2), 5.74(m, 1H), 6.86(d, 1H, 4-H), 7.50(d, 1H, 3-H). $J_{3\text{-}H,4\text{-}H}$ 4.0 Hz. (Found: C, 69.0; H, 7.93. $C_{12}H_{16}OS$ requires: C, 69.2; H, 7.74%).

2-Methacryloyl-5-phenylthiophen (7, R' = Ph), yield: 22% from 5-phenyl-2-propionylthiophen,[13] m.p. 87–88° (hexane). NMR($CDCl_3$): 2.08(s, 3H, CH_3), 5.78(bs, 1H, =CH), 5.83(bs, 1H, =CH), 7.3(m, 4H, aromatic), 7.6(m, 3H, aromatic). (Found: C, 73.3; H, 5.21. $C_{14}H_{12}OS$ requires: C, 73.6; H, 5.30%).

5-Methacryloyl-2-methylthiothiophen (7, R' = SMe), yield: 25% from 2-methylthio-5-propionylthiophen, purification by column chromatography (silica gel, pentane/ether, 90/10). NMR($CDCl_3$): 2.03(s, 3H, CH_3), 2.59(s, 3H, SCH_3), 5.75(m, 2H, =CH_2), 6.93(d, 1H, 3-H), 7.53(d, 1H, 4-H). $J_{3\text{-}H,4\text{-}H}$ 4.0 Hz. (Found: C, 54.0; H, 5.06. $C_9H_{10}OS_2$ requires: C, 54.5; H, 5.08%).

3-Series

4-Methacryloyl-2-methylthiophen (7, R' = Me), yield: 27% from 2-methyl-4-propionylthiophen, b.p.$_{2.6}$ 93–94°. NMR(CCl_4): 2.00(t, 3H, CH_3), 2.47(d, 3H, 2-CH_3), 5.75(m, 2H, =CH_2), 7.16(m, 1H, 3-H), 7.64(d, 1H, 5-H). $J_{3\text{-}H,5\text{-}H}$ 1.4 Hz, $J_{3\text{-}H,2\text{-}CH_3}$ 0.9 Hz. (Found: C, 64.97; H, 6.17. $C_9H_{10}OS$ requires: C, 65.03; H, 6.06%).

2-t-Butyl-4-methacryloylthiophen (7, R' = tBu), yield: 42% from 2-t-butyl-4-propionylthiophen, b.p.$_{0.3}$ 94–95°. NMR($CDCl_3$): 1.36(s, 9H, tBu), 2.00(t, 3H, CH_3), 5.72(pent., 2H, =CH_2), 7.24(d, 1H, 3-H), 7.69(d, 1H, 5-H). $J_{3\text{-}H,5\text{-}H}$ 1.4 Hz. (Found: C, 68.8; H, 8.16. $C_{12}H_{16}OS$ requires: C, 69.19; H, 7.74%).

4 - Methacryloyl - 2 - phenylthiophen (7, R' = Ph), yield: 26% from 2 - phenyl - 4 - propionylthiophen, m.p. 70.5–71.5° (hexane). NMR($CDCl_3$): 2.08(d, 3H, CH_3), 5.80(s, 2H, =CH_2), 7.2–7.8(m, 7H, aromatic). (Found: C, 73.6; H, 5.28. $C_{14}H_{12}OS$ requires: C, 73.6; H, 5.30%).

2 - Methylthio - 5 - propionylthiophen (5, R' = SMe 2-*isomer*). A mixture of 24.4 g (0.188 mol) of 2-methylthiothiophen and 29.3 g (0.225 mol) of propionic acid anhydride was stirred and heated to 60°, whereupon the heating was interrupted and 5.6 g of 85% ortho phosphoric acid was added dropwise. The temp. was not allowed to exceed 90°. The mixture was then heated to 100–110° for 3 hr, cooled, and 50 ml of water was added. After stirring for 1 hr the mixture was extracted with ether. The combined ethereal portions were washed with water, sat Na_2CO_3aq, water and dried ($MgSO_4$). After evaporation of the solvent, the residue was distilled, b.p.$_{0.4}$ 94–103°, yield 10.3 g (30%). NMR ($CDCl_3$): 1.19(t, 3H, CH_3), 2.58(s, 3H, SCH_3), 2.86(q, 2H, CH_2), 6.90(d, 1H, 3-H), 7.53(d, 1H, 4-H), J_{CH_3,CH_2} 6.5 Hz, $J_{3\text{-}H,4\text{-}H}$ 4.0 Hz. (Found: C, 51.3, H, 5.34. $C_8H_{10}OS_2$ requires: C, 51.6; H, 5.41%).

General description for the syntheses of the 3-propionylthiophenes 5. To a soln of the appropriate 2-substituted 4-bromo or 4-iodothiophen derivative in ether (100 ml/0.1 mol of thiophen derivative) 1.1 eq of BuLi in hexane was added at −70°, followed by 1.1 eq of N,N-dimethylpropionamide in ether (50 ml/0.1 mol of amide). The mixture was allowed to reach room temp. spontaneously by removal of the cooling bath. After stirring for 1 hr at room temp., excess 2N HCl was added and stirring was continued for 1 hr. The mixture was extracted with ether, the collected ethereal phases washed with water and dried. Evaporation of the solvent and distillation gave the 3-propionylthiophenes.

2-Methyl-4-propionylthiophen, yield: 64% from 4 - bromo - 2 - methylthiophen, b.p.$_{12}$ 114–116°. NMR($CDCl_3$): 1.17(t, 3H, CH_3), 2.45(d, 3H, 2-CH_3), 2.82(q, 2H, CH_2), 7.17(m, 1H, 3-H), 7.77(d, 1H, 5-H). $J_{3\text{-}H,5\text{-}H}$ 1.4 Hz, $J_{2\text{-}CH_3,3\text{-}H}$ 1.0 Hz, J_{CH_2,CH_3} 7 Hz. (Found: C, 62.39; H, 6.49. $C_8H_{10}OS$ requires: C, 62.30; H, 6.54%).

2-t-Butyl-4-propionylthiophen, yield: 67% from 2-t-butyl-4-iodothiophen,[17] b.p.$_{0.7}$ 91–93°. NMR($CDCl_3$): 1.17(t, 3H, CH_3), 1.35(s, 9H, tBu), 2.85(q, 2H, CH_2), 7.27(d, 1H, 3-H), 7.82(d, 1H, 5-H). $J_{3\text{-}H,5\text{-}H}$ 1.4 Hz, J_{CH_2,CH_3} 7 Hz. (Found: C, 67.2; H, 8.16. $C_{11}H_{16}OS$ requires: C, 67.30; H, 8.23%).

2-Phenyl-4-propionylthiophen, yield: 59% from 4-bromo - 2 - phenylthiophen,[18] m.p. 70–71.5° (EtOH). NMR($CDCl_3$): 1.20(t,

3H, CH_3), 2.88(q, 2H, CH_2), 7.3–7.6(m, 5H, C_6H_5), 7.66(d, 1H, 3-H or 5-H), 7.85(d, 1H, 3-H or 5-H). $J_{3\text{-}H,5\text{-}H}$1.4 Hz, $J_{CH_3CH_2}$7 Hz. (Found: C, 72.2, H, 5.49. $C_{13}H_{12}OS$ requires: C, 72.2; H, 5.59%).

2 - *Acryloyl* - 5 - *methylthiophen* 11). To 5.57 g (36.2 mmol) of 5 - methyl - 2 - propionylthiophen[15] in 100 ml of EtOAc, 8.6 g (45 mmol) of phenylselenenyl chloride was added, followed by 20 drops of conc HCl. The mixture was stirred at room temp. overnight. Tlc (silica, hexane/ethyl acetate 90/10) showed almost complete consumption of the starting material. Water was added and the organic layer was collected and washed with water, $NaHCO_3$aq and dried. Evaporation and distillation gave 7.7 g (69%) of the *α*-phenylseleno ketone, $b.p._{0.4}$ 145–155°, which was not completely pure (a small amount of diphenyl diselenide was present). This material (7.0 g, 23 mmol) was dissolved in 75 ml of THF, and 12.1 g (56.6 mmol) of sodium metaperiodate, dissolved in a minimum amount of water (*ca.* 50 ml), was added at room temp. The mixture was stirred for 2 hr and then extracted with ether. The ethereal phases were washed with water, dried and evaporated. Distillation gave pure 11, $b.p._{0.1}$ 57–62°, 1.7 g (49%). NMR($CDCl_3$): 2.85(s, 3H, CH_3), 5.82(ABq, 1H, =CH *trans*), 6.43(ABq, 1H, =CH *cis*), 7.08(ABq, 1H, –CH=), 6.83(d, 1H, 4-H), 7.58(d, 1H, 3-H). $J_{3,4\text{-}H}$3.0 Hz, $J_{=CH_2}$2.5 Hz, $J_{=CH\text{trans}\text{-}CH=}$ 10 Hz, $J_{=CH\text{cis}\text{-}CH=}$17 Hz. (Found: C, 63.22; H, 5.28. C_9H_8OS requires: C, 63.13; H, 5.30%).

Dipole moment determinations were performed as dielectric constant measurements (the resonance method) on benzene solutions of 1c and 2c at 21.6 ± 0.1° according to standard procedures.[19]

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