Oxidation and halogenation of methyl 4,5,6,7-tetrafluorobenzo[*b*]thiophen-2-carboxylate

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Abstract

4,5,6,7-Tetrafluorobenzo[*b*]thiophen-2-carboxylic acid (**IA**) was prepared by a modified literature procedure in two steps from pentafluorobenzaldehyde and rhodanine. Its methyl ester (**IB**) was synthesised via the acid chloride (**IC**) by reaction with methanol. Oxidation of **IB** with either CF_3CO_2H/H_2O_2 or *meta*-chloroperbenzoic acid gave methyl 2,3-dihydro-2,3-epoxy-4,5,6,7-tetrafluorobenzo[*b*]thiophen-1,1-dioxide-2-carboxylate (**II**). Methyl 2,3-dichloro-2,3-dihydro-4,5,6,7-tetrafluorobenzo[*b*]thiophen-2-carboxylate (**IIIA**) was prepared by reaction of **IB** either with chlorine, or with sulphuryl chloride and azobisisobutyronitrile.

Chloromethyl 4,5,6,7-tetrafluorobenzo[*b*]thiophen-2-carboxylate (**V**) was also produced with the latter reagents. Compound **IIIA** underwent thermal dehydrochlorination to give methyl 3-chloro-4,5,6,7-tetrafluorobenzo[*b*]thiophen-2-carboxylate (**IVA**), behaviour also observed during analyses involving gas chromatography. Treatment of **IB** with iodine pentafluoride in $CF_2ClCFCl_2$ and CF_3Cl gave, as shown by GLC, one major and several minor compounds. Analyses by coupled GLC–MS and GLC–IR methods indicated that the major product was **IVA**. Two of the minor products appeared to be methyl 3-iodo- (**IVB**) and methyl 3-fluoro-4,5,6,7-tetrafluorobenzo[*b*]thiophen-2-carboxylate (**IVC**). It is not known if these were produced during analysis or in the IF_5 reaction.

Introduction

1,4- [1] and 1,2- [2] Tetrafluorosulphobenzoic acids have been prepared as feedstocks for direct fluorination [3] studies. The *ortho*-diacid was synthesised [2, 3] by the oxidation of 4,5,6,7-tetrafluorobenzo[*b*]thiophen-2-carboxylic acid (**IA**). Several reactions of the methyl ester derivative (**IB**) are reported here.

General interest in benzo[*b*]thiophens derives from a wide range of biological and other activities and their chemistry has been comprehensively reviewed [4]. A number of 4,5,6,7-tetrafluorobenzo[*b*]thiophens variously substituted at C-2 and/or C-3 are known [5–9].

Results and discussion

4,5,6,7-Tetrafluorobenzo[*b*]thiophen-2-carboxylic acid (**IA**) is readily synthesised [10] in two steps from pentafluorobenzaldehyde. In the first step, reaction of pentafluorobenzaldehyde with rhodanine in the presence of a base affords 2,3,4,5,6-pentafluorobenzylidenerhodanine. Whereas the literature [10] preparation of the benzylidene derivative employs aqueous ammonium hydroxide/ammonium chloride, we obtained more reproducible results using triethylamine in chloroform. In the second step, treatment of the benzylidene with aqueous sodium hydroxide releases the masked thioalkoxide nucleophile which reacts intramolecularly to give **IA** [10]. The principle of intramolecular cyclisation by nucleophilic centres in side-chains of perfluoroaromatics is a well-established route to fused heterocyclic derivatives [5, 6, 11].

The methyl ester (**IB**) was prepared via the acid chloride (**IC**) by reaction with methanol. Spectral characterisation of **IB** and **IC** was consistent with the expected structures. Compounds **IB** and **IC** do not appear to have been cited previously in *Chemical Abstracts*.

Reaction of **IB** with either CF_3CO_2H/H_2O_2 or *meta*-chloroperbenzoic acid gave (Scheme 1) the epoxysulphone derivative **II**. The origin of **II** can be rationalised via oxidation of the sulphide of **IB** followed by epoxidation of the C2–C3 double bond. Literature analogy suggests that this is the probable sequence of oxidation. Stoichiometric reaction of peroxytrifluoroacetic acid with benzothiophen [12] appears to oxidise the sulphide group to a sulphone in preference to epoxidation of the double bond. Other oxidants, e.g. $EtCMe_2OOH/MoCl_5$ [13] and *meta*-chloroperbenzoic

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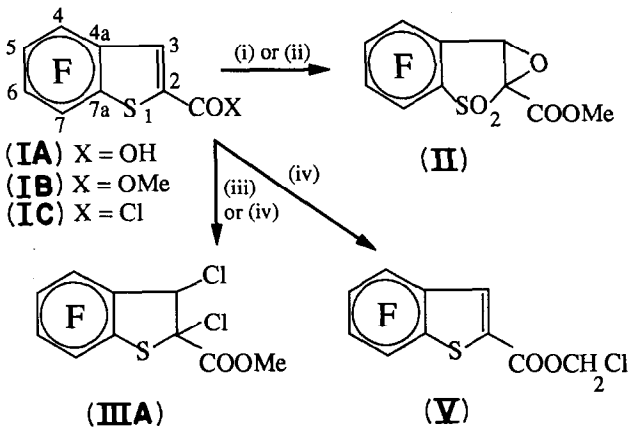


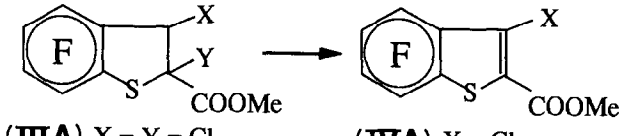
Scheme 1. Oxidation and chlorination of methyl 4,5,6,7-tetrafluorobenzo[*b*]thiophen-2-carboxylate (**IB**). (i) CF_3CO_2H/H_2O_2; (ii) *m*-$ClC_6H_4CO_3H$; (iii) Cl_2, Cl_3CCHCl_2; (iv) SO_2Cl_2, $[Me_2(CN)C-N=]_2$.

acid [14], have been reported to effect similar conversions.

Halogenations of **IB** with chlorine, with sulphuryl chloride (Scheme 1) and with IF_5 have been explored.

Treatment of **IB** with chlorine at 85 °C gave one major product which was purified by chromatography and was assigned, from spectral data, the structure methyl 2,3-dichloro-2,3-dihydro-4,5,6,7-tetrafluorobenzo[*b*]thiophen-2-carboxylate (**IIIA**). Gas and liquid-phase IR spectra of **IIIA** were similar apart from the ester carbonyl absorption which appeared at 1773 cm^{-1} in the gas phase and at 1756 cm^{-1} in the liquid phase. Similar fragmentation patterns, but with differences in relative intensities, were observed in the mass spectra of **IIIA** obtained either by the DI technique or by GLC–MS.

On heating to 250 °C, **IIIA** underwent smooth dehydrochlorination to give methyl 3-chloro-4,5,6,7-tetrafluorobenzo[*b*]thiophen-2-carboxylate (**IVA**). The IR ester carbonyl absorption of **IVA** appeared as a single peak at *c.* 1730 cm^{-1} in the spectrum recorded in the solid phase but as a 'doublet' at 1757 and 1731 cm^{-1} in the gas-phase spectrum (via GLC–IR–MS). The hydrocarbon analogue of **IVA** can be prepared [15] by heating $PhCH=CHCO_2Me$ with $SOCl_2$ and catalytic amounts of pyridine.



(**IIIA**) X = Y = Cl
(**IIIB**) X = I; Y unknown
(**IIIC**) X = F; Y unknown
(**IIID**) X = Cl; Y unknown

(**IVA**) X = Cl
(**IVB**) X = I
(**IVC**) X = F

Thermal dehydrohalogenation complicated gas chromatography analyses of products containing **IIIA** when HCl elimination occurred to varying degrees depending upon the injector ports, chromatography columns and temperatures employed.

Structure **IIIA** was produced in an independent experiment (Scheme 1). Sulphuryl chloride is a well-known chlorinating agent for allylic and benzylic carbons [16] and for the α-carbons of carbonyl compounds [16, 17]. Treatment of **IB** with sulphuryl chloride and azobisisobutyronitrile produced two major and several minor reaction products. In the absence of the radical initiator, the reproducibility of the reaction was variable with GLC estimated yields ranging from a few to *c.* 10%. Conversions were also not improved, when no radical initiator was present, by the separate addition of catalytic amounts of either $ZnCl_2$ or of pyridine. Column chromatographic purification of the reaction product gave an enriched fraction of the two major compounds, shown by NMR analysis to have the structure **IIIA** and **V** (chloromethyl 4,5,6,7-tetrafluorobenzo[*b*]thiophen-2-carboxylate). Infrared and mass spectra were obtained using the coupled GLC–IR–MS technique. Spectra for the first eluting GLC peak indicated either **IIIA** and/or **IVA** depending upon the analytical conditions and reflecting, as above, *in situ* dehydrochlorination during analysis. Spectra for the second eluting ('7.6 min') peak were consistent with structure **V**.

No reaction was observed when **IB** was treated with bromine in either CCl_4 or $CHCl_3$ at room temperature for 24 h.

The addition of mixed halogens across carbon–carbon double bonds using either single or 'mixed' reagents is well known [18–21]. Halogen fluorides, which have been extensively reviewed [22–25], may be thus employed when one of the elements is fluorine. Iodine fluorides (IF_n, e.g. $n = 1,3,5,7$) were of interest here.

A reagent, anticipated to be IF_5 together with some I_2, was prepared by reacting F_2 with I_2 in $CFCl_3$ at 0 °C and was then stored at room temperature. IF and IF_3 disproportionate above their boiling points of +1 °C and −35 °C to respectively I_2 and IF_5 and to IF, I_2 and IF_5. By contrast, IF_5 is a colourless liquid (b.p. 100 °C) stable at room temperature. IF_7 is made by reaction of IF_5 and F_2 at high (250 °C) temperatures. The elements of I and F have been added across double bonds either at low temperatures using IF [21] or by reaction of IF_5 and I_2 usually in the presence of a catalyst [24, 26].

The halogen reagent in $CFCl_3$ was reacted with a solution of **IB** in $CFCl_2CF_2Cl$. GLC analysis of the reaction products showed one major and several minor products. Infrared and mass spectral data were obtained using separate coupled GC–IR and GC–MS techniques.

Spectra for two of the minor compounds suggested structures **IVB** and **IVC**, reflecting the 3-iodo and 3-fluoro analogues of **IVA**. From the foregoing discussion, these compounds could arise either directly in the chemical reaction, or from a precursor (**III**) as a consequence of the analytical conditions employed (injector ports 250 °C). The latter possibility is rationalised by the anticipated addition of IF across the 2,3-double bond of **IB** and *in situ* dehydrohalogenation upon GLC analysis. The situation is however more complicated. Infrared and mass spectra for the major peak were identical with those obtained for **IVA** above. Common mass-spectral fragmentation patterns showing elimination of 'OCH_3', 'CO', 'CS' and 'halogen' (or HF) were seen for **IVA–C**. The individual IR spectra for the three compounds were identical across the width of the respective GLC peaks and showed, in the same manner as described above for **IVA**, 'doublets' for the ester carbonyl absorption. Assuming that **IVA–C** do arise via an elimination upon analysis, the nature of 'Y' in structure **IIIB–D** is thus unknown. Irrespective of the halogen reagent and the halogenation mechanism operating, the chlorine in **IVA** must originate in this reaction from the solvent.

The Cl_2 and SO_2Cl_2 halogenations described above were undertaken subsequent to the exploratory IF_5 reactions. Changes in our direction of work have left the latter study incomplete. Speculative results are offered here both for mechanistic implications and for possible investigation by other workers.

Experimental

General methods

GLC analysis

Analyses were undertaken using a Perkin-Elmer 8500 gas chromatograph fitted with a 25 m BP1 capillary column operating under one of the following programmes: (1) 100 °C for 1 min, 20 °C min^{-1} to 200 °C, 200 °C isothermal for 15 min; (2) 50–200 °C at 20 °C min^{-1}, 200 °C isothermal for an appropriate time.

Coupled GLC–IR–MS analyses were undertaken using a Hewlett Packard 5890 series 1 gas chromatograph coupled in series with a FT 5965A IR spectrophotometer and a 5971 mass spectrometer. On-column injections were made into a 0.5 m × 0.53 mm deactivated fused silica coatless glass tube connected to a 12.5 m × 0.32 mm CP SIL 5CB column (0.25 μm film thickness) programmed for 1 min at 60 °C then ramped at 5 °C min^{-1} to an appropriate temperature.

Other general methods have been reported [1] previously.

2,3,4,5,6-Pentafluorobenzylidenerhodanine

Triethylamine (38.0 g, 0.38 mol) was added to a well-stirred suspension of rhodanine (50.0 g, 0.38 mol) in a solution of pentafluorobenzaldehyde (70 g, 0.36 mol) in chloroform at such a rate that the temperature did not rise above *c.* 40 °C. The homogeneous solution produced was stirred at room temperature for 1 h, then washed successively with cold HCl (2 × 60 ml of 1:3 conc. HCl H_2O) and water (2 × 60 ml). The solvent was removed under reduced pressure at *c.* 40 °C and the yellow residue (131 g) was recrystallised from ethanol/water to give the title compound (82 g), m.p. 132–135 °C (lit. value [10], 135 °C).

4,5,6,7-Tetrafluorobenzo[b]thiophen-2-carboxylic acid (IA)

The benzylidene derivative from above (78.8 g, 0.25 mol) was added in small portions to a stirred solution of NaOH (68 g, 1.7 mol) in water (300 ml) at *c.* 40 °C. The clear pale red solution obtained was heated to 90 °C and stirred at this temperature for 1 h. On reaching *c.* 70 °C, a cream coloured precipitate separated. The mixture was then chilled in ice, acidified (conc. HCl), filtered and washed. Care must be taken to ensure total neutralisation which is often inhibited by the agglomerated precipitate. Drying over P_2O_5 under vacuum afforded the crude product (59 g) which was purified by sublimation to give the title compound (51.6 g), m.p. 200 °C (lit. value [10], 199–200 °C, dec.). For NMR data, see Table 1 and ref. 27.

Methyl 4,5,6,7-tetrafluorobenzo[b]thiophen-2-carboxylate (IB)

The benzothiophen-2-carboxylic acid (**IA**, 5.0 g, 20 mmol) was refluxed for 1 h with excess $SOCl_2$ (10 g, 84 mmol). Total solution was obtained after *c.* 20 min. Excess $SOCl_2$ was removed under reduced pressure leaving as a pale yellow oil 4,5,6,7-tetrafluorobenzo[*b*]thiophen-2-carbonyl chloride (**IC**) (5.5 g). For NMR data, see Table 1. MS *m/z*: 268 (22%, M^+); 233 (100); 205 (27); 161 (70). IR (film) ν_{max} (cm^{-1}): 1745 (s); 1650 (w); 1430 (m); 1420 (m); 1400 (s); 1380 (s); 1365 (s); 1175 (s); 1140 (s); 1090 (m); 1080 (m); 1000 (s); 880 (m); 840 (m); 800 (m); 760 (m). Dry methanol (7.5 g) was added to the acid chloride and the mixture was refluxed for 10 min. Volatiles were removed under reduced pressure and the residue (5.56 g) was recrystallised from ethanol/water to give the title compound (4.8 g, 91%), m.p. 96–97 °C. For NMR data, see Table 1. MS *m/z*: 264 (65%, M^+); 233 (100); 205 (23); 161 (70). IR (KBr) ν_{max} (cm^{-1}): 1725 (s); 1540 (m); 1495 (s); 1435 (m); 1365 (m); 1260 (s); 1250 (s); 1145 (m); 1075 (m); 995 (m); 945 (w); 878 (m); 775 (w); 760 (w). GLC analysis (programme 1) showed a single peak eluting at 4.8 min.

TABLE 1. NMR data for derivatives of 4,5,6,7-tetrafluorobenzo[*b*]thiophen-2-carboxylic acid (**IA**)

Structure	Substituents	Solvent	Nuc	$-S^1-C^2(COX)-C^3-C_6F_4-$ [*b*]								
	$-S^1-C^2(COX)-C^3-$			2 (*J*, Hz)	3 (*J*, Hz)	4a (*J*, Hz)	4 (*J*, Hz)	5 (*J*, Hz)	6 (*J*, Hz)	7 (*J*, Hz)	7a (*J*, Hz)	−COX (*J*, Hz)
IA	$-S-C(CO_2H)=CH-$	$(CD_3)_2CO$	F	–	–	–	−142.6 (19×16×3) (d×d×d)	−157.0 (19×2) (t×d)	−160.0 (19) (t)	−142.8 (19×16×3) (d×d×d)	–	–
		$(CD_3)_2CO$	H	–	8.2 (1H,d,3)	–	–	–	–	–	–	8.7 (1H,s,−OH)
IB	$-S-C(CO_2Me)=CH-$	$CDCl_3$	F	–	–	–	−141.0 (19×16×3) (d×d×d)	−155.7 (19×2) (t×d)	−159.0 (19) (t)	−142.6 (19×16×3) (d×d×d)	–	–
			H	–	8.0 (1H,d,3)	–	–	–	–	–	–	3.9 (3H,s,$-OCH_3$)
			C	136.2	124.6	[124.3 or 125.1][a] (d)	[141.4 or 143.0] (d×d)	[138.0 or 140.0] (d×t)	[138.0 or 140.0] (d×t)	[141.4 or 143.0] (d×d)	[124.3 or 125.1] (d)	161.2
IC	$-S-C(COCl)=CH-$	$CDCl_3$	F	–	–	–	−139.9 (19×16×3) (d×d×d)	−151.8 (19×3) (t×d)	−157.2 (19) (t)	−140.6 (19×16×3) (d×d×d)	–	–
			H	–	8.3 (d,3)	–	–	–	–	–	–	–
			C	139.6	129.4	[126.8 or 124.1] (d)	[141.5 or 143.5] (d×d)	[138.9 or 141.0] (d×t)	[138.9 or 141.0] (d×t)	[141.5 or 143.5] (d×d)	[126.8 or 124.1] (d)	159.9
II	$-SO_2-C(CO_2Me)(O)CH-$	$CDCl_3$	F	–	–	–	−137.2 (22×16.2×7.5×1.5) (d×d×d×d)	−144.5 (22.5×17.5×6.2) (d×d×d)	−143.8 (21.2×17.5×7.5) (d×d×d)	−141.6 (21.2×16.2×6.2) (d×d×d)	–	–
			H	–	4.95 (1H,d,1.5)	–	–	–	–	–	–	3.95 (3H,s,−OMe)
			C	70.5 (s)	[53.6 or 54.5] (s)	[115.2 or 123.3] (d)	[143.5 or 145.8] (d×d)	[142.8 or 144.0] (d×t)	[142.8 or 144.0] (d×t)	[143.5 or 145.8] (d×d)	[115.2 or 123.3] (d)	159.8 [53.6 or 54.5] (s,$-OCH_3$)
IIIA	$-S-CCl(CO_2Me)-CCl-$	$CDCl_3$	F	–	–	–	−137.4 (20×13.8×1.8) (d×d×d)	−150.1 (20×5.0) (t×d)	−156.1 (20.0) (t)	−138.4 (20×13.8×5.0) (d×d×d)	–	–
			H	–	5.65 (1H,d,1.8)	–	–	–	–	–	–	3.90 (3H,s)
			C	88.9 (s)	64.5 (s)	[120.2 or 121.7] (d)	[143.0 or 144.6] (d×d) (d×d×d)	[139.4 or 142.7] (d×t) (d×t×d)	[139.4 or 142.7] (d×t) (d×t×d)	[143.0 or 144.6] (d×d) (d×d×d)	[120.2 or 121.7] (d)	163.5 (s) 54.4 (s,−OMe)
IVA	$-S-C(CO_2Me)=CCl-$	$CDCl_3$	F	–	–	–	−142.2 (19.5×15.9) (d×d)	−153.9 (19.5×3.7) (t×d)	−157.3 (19.5) (t)	−146.1 (19.5×15.9×3.7) (d×d×d)	–	–
			H	–	–	–	–	–	–	–	–	4.0 (s,−OMe)
			C	125.2	128.3	[122.3 or 122.6] (d)	[141.3 or 143.4] (d×d)	[139.2 or 139.9] (d×t)	[139.2 or 139.9] (d×t)	[141.3 or 143.4] (d×d)	[122.3 or 122.6] (d)	160.1 (52.8, −OMe)
V	$-S-C(CO_2CH_2Cl)=CH-$	$CDCl_3$	F	–	–	–	−140.5 (18.8×6.3×3) (d×d×d)	−154.3 (18.8×2.5) (t×d)	−158.3 (18.8) (t)	−141.8 (18.8×16.3×3) (d×d×d)	–	–
			H	–	8.2 (1H,d,3)	–	–	–	–	–	–	5.95 (2H,s,$-CH_2Cl$)

[a][] square brackets denote uncertain assignment between signals bracketed.
[b]Numbering system illustrated in structure I of Scheme 1.

Methyl 2,3-dihydro-2,3-epoxy-4,5,6,7-tetrafluorobenzo[b]thiophen-1,1-dioxide-2-carboxylate (II)

(a) By reaction of IB with CF_3CO_2H/H_2O_2

Hydrogen peroxide (30% w/w, 7.0 g, 61.8 mmol) was added in small portions to a stirred solution of the methyl benzothiophen-2-carboxylate (**IB**, 0.91 g, 3.5 mmol) in trifluoroacetic acid (7 ml) at 40 °C. The precipitate which was produced on each addition rapidly dissolved. The mixture was stirred for 4 h at room temperature when volatiles were removed under a stream of nitrogen and the residue taken up in dichloromethane and washed with water. The organic phase was separated, dried ($MgSO_4$) and the solvent evaporated affording a solid (0.72 g) which was recrystallized from chloroform/hexane to give the title compound (0.35 g), m.p. 120–122 °C. For NMR data, see Table 1. MS *m/z* (DI, probe 200 °C): 312 (M^+, 43%); 248 (6); 225 (18); 217 (100); 209 (22); 205 (54); 190 (12); 181 (10); 177 (12); 161 (83); 149 (13); 148 (8); 141 (8); 137 (14); 123 (13); 111 (11); 99 (18); 93 (21); 75 (12); 69 (9); 59 (68). IR (KBr) ν_{max} (cm^{-1}): 3434 (w); 3084 (w); 2968 (w); 1756 (s); 1636 (w); 1508 (s); 1442 (m); 1396 (m); 1356 (s); 1324 (s); 1268 (m); 1234 (m); 1182 (s); 1146 (w); 1106 (w); 988 (m); 940 (w); 926 (w); 856 (w); 796 (w); 760 (w); 743 (w); 670 (w); 650 (w); 586 (m); 568 (m).

(b) By reaction of IB with m-chloroperbenzoic acid

A mixture of methyl 4,5,6,7-tetrafluorobenzo[*b*]-thiophen-2-carboxylate (**IB**, 1.32 g, 5 mmol) and *m*-chloroperbenzoic acid (6.6 g, 30 mmol at 80% purity) in methylene chloride (50 ml) was heated under reflux for 8 h. The reaction mixture was worked-up as described above to give the title compound.

Methyl 2,3-dichloro-2,3-dihydro-4,5,6,7-tetrafluorobenzo[b]thiophen-2-carboxylate (IIIA)

A fine steam of chlorine gas was bubbled for 20 min through a solution of **IB** (1.04 g, 3.94 mmol) in pentachloroethane (5 ml) at 85 °C. The mixture was heated at 130 °C for 30 min. Volatiles were removed under reduced pressure and the residue (1.1 g) was purified by column chromatography (BDH 60–120 mesh silica gel, 8% chloroform/hexane eluent) to give the title compound as an oil (0.65 g). For NMR data, see Table 1. MS *m/z* (DI, probe at 200 °C): 338 (5%); 336 (6); 334 (M^+, 38%); 298 (5); 277 (6); 275 (10); 267 (7); 264 (21); 255 (11); 242 (37); 240 (100); 233 (48); 205 (18); 161 (83); 111 (12); 93 (11); 87 (9); 69 (8); 59 (81). IR (film) ν_{max} (cm^{-1}): 3008 (w); 2960 (w); 1756 (s); 1636 (w); 1498 (s); 1438 (m); 1382 (m); 1275 (s); 1232 (m); 1138 (m); 1062 (s); 1032 (m); 976 (m); 908 (w); 864 (m); 832 (w). Similar analysis by GLC–IR–MS (on-column injection) IR (gas phase) ν_{max} (cm^{-1}) gave 2966 (5.66 mAU); 1773 (30.21); 1633 (3.11); 1498 (93.39); 1442 (7.35); 1379 (8.27); 1267 (37.81); 1138 (10.55); 1065 (17.17); 977 (8.24); 864 (9.83); 833 (5.73); 761 (6.63); 666 (7.66).

Under certain conditions, GLC–IR–MS analysis of a pure sample of **IIIA** showed, in addition to **IIIA**, several well-resolved peaks, each giving identical spectra indicating structure **IVA**. This behaviour was rationalised by dehydrochlorination of **IIIA** at different points in the injector port or on the chromatography column. Gas-phase spectra of **IIIA** were best obtained by on-column injections using column temperatures below 130 °C. Injection of a pure sample of **IIIA** through a port at 170 °C (programme 2) gave two peaks corresponding to **IIIA** and **IVA**. When the injector ports were heated at 250 °C, total dehydrochlorination was usually observed.

Methyl 3-chloro-4,5,6,7-tetrafluorobenzo[b]thiophen-2-carboxylate (IVA)

Methyl 2,3-dichloro-2,3-dihydro-4,5,6,7-tetrafluorobenzo[*b*]thiophen-2-carboxylate (**IIIA**, 175 mg, 0.52 mmol) was heated under nitrogen at 250 °C for 20 min. The product was dissolved in CH_2Cl_2 and filtered through BDH 60–120 mesh silica gel. Evaporation of the solvent from the filtrate afforded a residue (170 mg) which was recrystallised from ethanol/water to give the title compound (149 mg), m.p. 105–106 °C. For NMR data, see Table 1. IR (KBr) ν_{max} (cm^{-1}): 2964 (w); 1730 (s); 1650 (w); 1524 (s); 1496 (s); 1476 (m); 1434 (m); 1354 (s); 1322 (w); 1244 (s); 1202 (m); 1106 (s); 1074 (m); 1004 (m); 966 (w); 885 (m); 862 (s); 764 (w); 646 (w). Analysis by GLC–IR–MS gave *m/z* 300 (27%); 298 (74, M^+); 295 (9); 269 (37); 268 (11); 267 (100); 241 (12); 240 (6); 239 (32); 204 (13); 197 (9); 195 (30); 160 (9); 135 (5) and ν_{max} (gas phase, mAU cm^{-1}) 2965 (5.64); 1757 (23.92); 1731 (18.78); 1647 (5.02); 1522 (30.86); 1498 (51.39); 1439 (8.19); 1354 (29.87); 1283 (25.73); 1236 (47.26); 1200 (13.93); 1110 (26.57); 1078 (14.40); 1017 (2.96); 929 (3.46); 888 (12.38). GLC analysis (programme 2) showed a single peak eluting at 7.8 min.

Chloromethyl 4,5,6,7-tetrafluorobenzo[b]thiophen-2-carboxylate (V) (together with IIIA)

A mixture of methyl 4,5,6,7-tetrafluorobenzo[*b*]-thiophen-2-carboxylate (**IB**, 1.13 g, 4.28 mmol) and azo-bis-isobutyronitrile (0.24 g, 1.46 mmol) in sulphuryl chloride (11.7 g, 86.7 mmol) was refluxed for 1 h and left at room temperature for 20 h. Volatiles were removed under reduced pressure and the residue was taken up in diethyl ether and washed with water. Evaporation of the solvent from the dried ($MgSO_4$) extract afforded a gum (1.1 g) which was purified by column chromatography (BDH 60–120 mesh silica gel,

5% $CHCl_3$ in hexane eluent) to give an enriched mixture (0.62 g) of two compounds shown by NMR analysis (see Table 1) to be methyl 2,3-dichloro-2,3-dihydro-4,5,6,7-tetrafluorobenzo[*b*]thiophen-2-carboxylate (**IIIA**) and the title compound (**V**). Compounds **IIIA** and **V** were present in a mole ratio of 1:2.2, respectively. GLC analysis (programme 2) showed peaks eluting at 7.1 (structure **IIIA**) [and/or 7.8 min (structure **IVA**) depending upon analytical conditions – see above] and 7.6 min (structure **V**). Combined GC–IR–MS of the first (7.1 min) eluting peak gave spectra identical with those seen above for methyl 2,3-dichloro-2,3-dihydro-4,5,6,7-tetrafluorobenzo[*b*]thiophen-2-carboxylate (**IIIA**). Combined GC–IR–MS of the second eluting (7.6 min) peak gave *m/z* 298 (M^+, 27%); 235 (5); 234 (11); 233 (100); 206 (7); 205 (23); 162 (5); 161 (66); 93 (5) and ν_{max} (gas phase, mAU cm^{-1}) 2996 (5.5); 1760 (101.1); 1649 (11.3); 1536 (46.6); 1495 (160.5); 1363 (43.2); 1262 (62.1); 1219 (182.4); 1146 (79.3); 1062 (162.2); 1004 (36.9); 960 (11.9); 876 (36.7); 759 (28.8) consistent with the structure for chloromethyl 4,5,6,7-tetrafluorobenzo[*b*]thiophen-2-carboxylate (**V**).

Reaction of methyl 4,5,6,7-tetrafluorobenzo[b]thiophen-2-carboxylate (**IB**) with IF_5 *in* $CFCl_2CF_2Cl/CFCl_3$

Fluorine gas (16% in nitrogen) was bubbled slowly through a stirred suspension of I_2 (20.0 g, 78.8 mmol) in $CFCl_3$ (100 ml) at 0 °C until a faintly pink clear solution was obtained. The product was kept at room temperature for 1 week before use. A stirred mixture of the benzothiophen methyl ester (**IB**, 0.2 g, 0.76 mmol), $CFCl_2CF_2Cl$ (2 ml) and a solution of iodine pentafluoride (0.5 g, 2.3 mmol) in $CFCl_3$ (*c.* 2.5 g) was refluxed under nitrogen for 2 h and left at ambient temperature for 6 d. Volatile material was removed under reduced pressure and the residue extracted with chloroform. GLC analysis (programme 2) of the chloroform extract showed one major peak eluting at 7.8 min and several minor peaks including those eluting at 6.6, 7.1 and 9.1 min respectively. The 6.6 min peak was identified as unreacted benzothiophen **IB**.

Combined GLC–MS and GLC–IR analyses of the 7.8 min peak gave respectively *m/z* 298 (M^+, 68%); 267 (100); 239 (34); 204 (18); 195 (40); 160 (15); 135 (9); 119 (5); 111 (8); 102 (7) and ν_{max} (gas phase, mAU, cm^{-1}) 1755 (0.21); 1731 (0.18); 1522 (0.30); 1499 (0.45); 1354 (0.28); 1284 (0.25); 1237 (0.43); 1201 (0.14); 1110 (0.24); 1079 (0.14); 888 (0.13); 868 (0.11) indicating methyl 3-chloro-4,5,6,7-tetrafluorobenzo[*b*]thiophen-2-carboxylate (**IVA**).

Similar analyses for the 7.1 min peak gave respectively *m/z* 282 (M^+, 68%); 251 (100); 223 (34); 179 (78); 177 (15); 59 (38) and ν_{max} (gas phase, mAU, cm^{-1}) *c.* 2965; 1763 (0.07); *c.* 1740; 1500 (0.19); 1404 (0.07); 1272 (0.08); 1232 (0.07) suggesting the structure methyl 3-fluoro-4,5,6,7-tetrafluorobenzo[*b*]thiophen-2-carboxylate (**IVC**).

Similar analysis for the 9.1 min peak gave respectively *m/z* 390 (M^+, 100%); 359 (73); 331 (21); 233 (10); 204 (50); 192 (12); 160 (22); 135 (14); 127 (12); 111 (10); 59 (10) and ν_{max} (gas phase, mAU, cm^{-1}) 2965 (0.03); 1752 (0.06); 1731 (0.05); 1647 (0.03); 1499 (0.13); 1437 (0.03); 1337 (0.06); 1276 (0.06); 1226 (0.11); 1103 (0.06); 1072 (0.04); 1003 (0.03); 925 (0.03); 890 (0.04); 818 (0.04); 798 (0.03) suggesting the structure methyl 3-iodo-4,5,6,7-tetrafluorobenzo[*b*]thiophen-2-carboxylate (**IVB**).

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