Studies on Sulphur Heterocycles. Reactions of 6,7-Dihydrobenzo[*b*]thiophen-4(5*H*)one Derivatives and their Conversion to 7-Substituted Thieno[2,3-*h*][1]benzopyran-8-ones

Chris M. Asprou, John S. A. Brunskill, Howard Jeffrey*

Department of Chemistry, UWIST, Cardiff CF1 3NU, Wales, U.K.

and

*Asish De**

School of Physical Sciences, New University of Ulster, Coleraine, Northern Ireland BT52 1SA

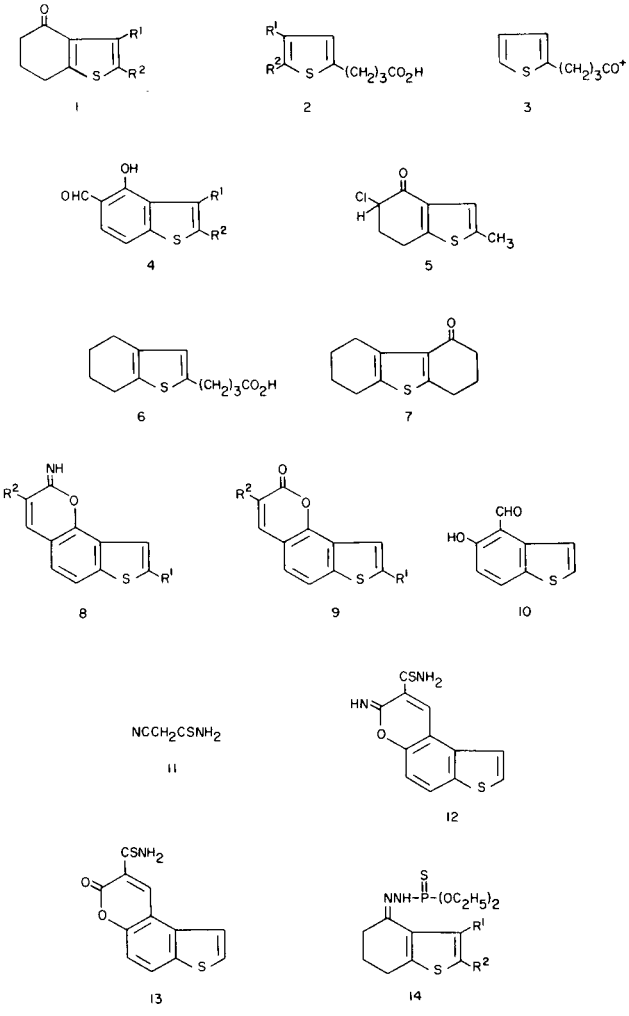
Received August 15, 1979

Cyclization of γ-(2-thienyl)butyric acid with acid anhydrides gives 2-acyl derivatives as well as the expected 6,7-dihydrobenzo[*b*]thiophen-4(5*H*)one. Several reactions of these ketones have been studied including their conversion to 0,0-diethyl thiophosphonohydrazones. 7-Substituted thieno[2,3-*h*][1]benzopyran-8-ones have been prepared *via* 4-hydroxybenzo[*b*]thiophen-5-carbaldehydes.

J. Heterocyclic Chem., **17**, 87 (1980).

6,7-Dihydrobenzo[*b*]thiophene-5(5*H*)one (**1**, $R^1 = R^2 = H$) (1) has been reported as a key intermediate in the syntheses of sulphur analogues of furocoumarins (2). The medicinal properties of naturally occurring furocoumarins (3) had led to the synthesis of their sulphur analogues for investigation of structure-activity relationships (2,4,5) and recent reports of the nmr spectra (6,7) of furocoumarins have also promoted our interest in the thiophen derivatives. So our studies of coumarins (8), prepared principally for spectroscopic correlations and pharmacological and anti-microbial screening, have been continued to include certain thieno[2,3-*h*]coumarins (**9**). These are obtained by acid hydrolysis of the corresponding imines (**8**) which result from the condensation of active cyanomethylene compounds with the appropriate substituted 4-hydroxybenzo[*b*]thiophen-5-carbaldehyde (**10**). This is produced by formylation (9) and dehydrogenation (10) of the cyclic ketone (**1**).

The unsubstituted ketone (**1**, $R^1 = R^2 = H$) had previously been prepared from γ-(2-thienyl)butyric acid (**2**, $R^1 = R^2 = H$) through the acid chloride (11) or by treatment with boiling acetic anhydride in the presence of polyphosphoric acid (12). The second method apparently involves the intermediacy of the oxocarbonium ion (**3**) generated by the action of polyphosphoric acid on the mixed anhydride of acetic and γ-(2-thienyl)butyric acids, as in normal Friedel-Crafts acylations (13). Steric factors direct the attack by this cation on the less reactive adjacent β-position, leaving the free more reactive 2-position accessible to acylation by any acetyl cation present in the reaction medium. However, no report in the literature has been found of the formation of the expected acylated product of this cyclization (14), 2-acetyl-6,7-dihydrobenzo[*b*]-thiophen-4(5*H*)one (**1**, $R^1 = H$, $R^2 = COCH_3$). Nevertheless, from an unsuccessful attempt to prepare 3-methyl-



6,7-dihydrobenzo[*b*]thiophen-4(5*H*)one (**1**, $R^1 = CH_3$, $R^2 = H$) from γ-(4-methyl-2-thienyl)butyric acid (**2**, $R^1 = CH_3$, $R^2 = H$) only the 2-acetyl derivative (**1**, $R^1 = CH_3$,

0022-152X/80/010087-06$02.25

$R^2 = COCH_3$) had been isolated (15). Since no other example of this side reaction has been reported, the cyclization of the unsubstituted acid (**2**, $R^1 = R^2 = H$) was re-examined to verify whether the acetyl derivative (**1**, $R^1 = H$, $R^2 = COCH_3$) was formed, but removed subsequently on purification of the major product (**1**, $R^1 = R^2 = H$). Thin layer chromatography (light petroleum:ethyl acetate = 7:3) of the cyclized material prior to recrystallisation showed, in addition to the reported product (12) (**1**, $R^1 = R^2 = H$; R_f 0.6) another (R_f 0.4), which reacted with 2,4-dinitrophenylhydrazine. The infrared spectrum of the crude mixture also contained; as well as the band at 1676 cm^{-1}, a second in the carbonyl region at 1665 cm^{-1}. The nmr spectrum exhibited, besides the resonances of the unsubstituted ketone (16), a singlet at δ 7.9 (1H), three multiplets at δ 3.1 (2H), 2.7 (2H) and 2.25 (2H) and a sharp singlet at δ 2.6 (3H). The presence of the 2-acetyl derivative (**1**, $R^1 = H$, $R^2 = COCH_3$) was confirmed, when it was isolated by hplc (light petroleum:ethyl acetate = 4:1) as 20% of the product. It was prepared also by acetylating the unsubstituted ketone (**1**, $R^1 = R^2 = H$) with acetic anhydride in the presence of polyphosphoric acid.

Subjecting aliquots taken from the reaction mixture during cyclization (of **2**, $R^1 = R^2 = H$) to tlc showed the unsubstituted ketone (**1**, $R^1 = R^2 = H$) to be formed first followed by acetylation. This second reaction could be delayed significantly at lower temperatures, but the yield of unsubstituted ketone was poor, much unchanged acid being recovered. However, 35% could be attained with very little by-product using anhydrous aluminium chloride instead of polyphosphoric acid. With propanoic or hexanoic anhydride and polyphosphoric acid under reflux higher yields of the 2-acyl derivatives (**1**, $R^1 = H$, $R^2 = COCH_2CH_3$ or $CO(CH_2)_4CH_3$) resulted but with trifluoroacetic anhydride no acylated product was detected, although the yield of unsubstituted ketone was only 15%. Thus the previous failure (15) to obtain 3-methyl-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)one (**1**, $R^1 = CH_3$, $R^2 = H$) was apparently due to its conversion to the 2-acetyl derivative at the high cyclization temperature employed, since, indeed, it could be isolated as the minor product from a reaction at 36°.

γ-(5-Methyl-2-thienyl)butyric acid (**2**, $R^1 = H$, $R^2 = CH_3$) on treatment with acetic anhydride and polyphosphoric acid gave only 2-methyl-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)one (**1**, $R^1 = H$, $R^2 = CH_3$) which could not be acylated with acetic anhydride. Nor could the 2-bromo-derivative (**1**, $R^1 = H$, $R^2 = Br$) under identical conditions. Although a substituted thiophen with an electron withdrawing group in the 4-position can be acetylated in the 3-position (17), the carbonyl function in the ketone (**1**) appears capable of deactivating the 3-position towards acetylation through inductive and mesomeric effects, but not towards the attack of the more powerful electrophile involved in nitration.

Nitration of the 2-bromo derivative (**1**, $R^1 = H$, $R^2 = Br$) in the 3-position had been described (12), and the 2-methyl derivative (**1**, $R^1 = H$, $R^2 = CH_3$) has been nitrated in the 3-position under the same conditions while the unsubstituted ketone (**1**, $R^1 = R^2 = H$) is attacked in the 2-position.

The expected reactivity towards nucleophiles of the bromine atom in 2-bromo-3-nitro-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)one (**1**, $R^1 = NO_2$, $R^2 = Br$) is exemplified in the preparation of the thioglycolic ester (**1**, $R^1 = NO_2$, $R^2 = SCH_2CO_2CH_3$) by the action of sodium methoxide and methyl thioglycollate. Attempts to chlorinate the un-

Table I

Physical Constants of 7-Substituted Thieno[2,3-*h*][1]benzopyran-8-ones (**9**)

R^1	R^2	Cyanomethylene Compound used	Yield %	M.p. (a,b)	Molecular Formula	Analysis Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
H	CN	Malononitrile	62	260°	$C_{12}H_{15}NO_2S$	63.4	2.2	6.2	63.3	2.3	5.9
H	$CONH_2$	Cyanoacetamide	30	308°	$C_{12}H_7NO_3S$	58.8	2.9	5.7	58.8	3.2	6.0
H	$COCH_3$	Methyl cyanoacetate	47	180-181°	$C_{13}H_{10}O_4S$	60.0	3.1	—	60.0	3.1	—
H	$CO_2C_2H_5$	Ethyl Cyanoacetate	52	132-133°	$C_{14}H_{10}O_4S$	61.3	3.7	—	61.3	3.6	—
CH_3	CN	Malononitrile	68	253°	$C_{13}H_7NO_2S$	64.6	3.0	5.7	64.7	2.9	5.8
CH_3	$CSNH_2$	(c)	33	269°	$C_{13}H_9NO_2S_2$	56.7	3.3	5.1	56.7	3.3	5.1
CH_3	CO_2CH_3	Methyl cyanoacetate	43	210°	$C_{14}H_{10}O_4S$	61.3	3.7	—	61.0	3.8	—
CH_3	$CO_2C_2H_5$	Ethyl cyanoacetate	48	163-164°	$C_{15}H_{12}O_4S$	62.5	4.3	—	62.5	4.2	—
Br	CN	Malononitrile	64	311°	$C_{12}H_{14}BrNO_2S$	46.9	1.4	4.6	47.2	1.3	4.6
Br	$CONH_2$	Cyanoacetamide	32	330°	$C_{12}H_6BrNO_3S$	44.6	1.9	3.8	44.4	1.9	4.3
Br	$CSNH_2$	(c)	33	255°	$C_{12}H_6BrNO_2S_2$	42.8	1.9	4.3	42.4	1.8	4.1
Br	CO_2CH_3	Methyl Cyanoacetate	55	266°	$C_{13}H_7BrO_4S$	46.3	2.2	—	46.0	2.1	—
Br	$CO_2C_2H_5$	Ethyl Cyanoacetate	57	183°	$C_{14}H_9BrO_4S$	47.5	2.6	—	47.6	2.6	—

(a) Recrystallized from ethanol. (b) Decomposed on melting. (c) Obtained by thiolysis of the nitrile.

substituted ketone (**1**, $R^1 = R^2 = H$) with *N*-chlorosuccinimide in boiling carbon tetrachloride produced intractable tars, but the 2-methyl derivative (**1**, $R^1 = H$, $R^2 = CH_3$) has been chlorinated in the 5-position under the same conditions. The ir and nmr spectra indicate that the product (5) exists entirely in the keto-form. Monosuccinoylation of the simple ketone (**1**, $R^1 = R^2 = H$) with succinic anhydride and anhydrous aluminium chloride in boiling dichloro-methane gave the γ-ketoacid (**1**, $R^1 = H$, $R^2 = CO(CH_2)_2CO_2H$) in which both keto-groups were reduced by the Huang-Minlon procedure to yield γ-2-(4,5,6,7-tetrahydrobenzo[*b*]thienyl)butyric acid. The cyclization with acetic anhydride afforded 1,2,5,6,7,8-hexahydrodibenzo-[*b*]thiophen-4(3*H*)one which had previously been prepared through the acid chloride (of **6**) (18).

The physical constants and spectroscopic data of the 7-substituted thieno[2,3-*h*][1]benzopyran-8-ones (**9**) are summarised in Tables 1 and 2. Although the thieno[3,2-*f*]-[1]benzopyran-7-one-8-thiocarboxamide (**13**) had been prepared (8) by condensing 5-hydroxybenzo[*b*]thiophen-4-carbaldehyde (**10**) with 2-cyanthioacetamide (**11**) followed by acid hydrolysis of the imine (**12**), the isomeric thiocarboxamides (**9**, $R^3 = CSNH_2$) could not be obtained following this method. The nitriles (**9**, $R^1 = H$, $R^2 =$ Br or CH_3), however, underwent smooth thiolysis with hydrogen sulphide (19) in the presence of triethyl amine to give the desired compounds.

Benzo[*b*]thiophen derivatives with a thiophosphonate side-chain in the 4-position are known pesticides (19). The *O,O*-diethyl thiophosphono hydrazones (**14**) have been prepared from the cyclic ketones (**1**) for biological evaluation. The physical constants and spectroscopic data of these compounds are described in Tables 3 and 4.

EXPERIMENTAL

Melting points are uncorrected. Nmr spectra were recorded in a Perkin-Elmer R-32 instrument using tetramethyl silane as internal standard and deuterochloroform as solvent unless otherwise stated. Ir spectra were recorded in a Perkin-Elmer instrument as potassium bromide discs, unless otherwise stated. Light petroleum has boiling point 60-80°.

Cyclization of γ-(2-Thienylbutyric Acid) (**2** $R^1 = R^2 = H$).

(a) With Acetic Anhydride and Polyphosphoric Acid.

γ-(2-Thienyl)butyric acid (5 g.) (11) acetic anhydride (30 ml.) and polyphosphoric acid (1 ml.) were refluxed for one hour. After cooling, the reaction mixture was added to crushed ice and extracted with ether. The etherial extract after washing successively with 5% sodium bicarbonate and water was dried over anhydrous sodium sulphate. The syruppy residue left after the evaporation of the solvent, yielded on vacuum distillation a fraction boiling at 82-83°/1 mm which solidified on cooling. Hplc of the distillate (3.5 g.) using light petroleum:ethyl acetate (4:1) gave 6.7 dihydrobenzo[*b*]thiophen-4(5*H*)one **1** ($R^1 = R^2 = H$) (2.6 g., 74% of the mixture, 60% overall yield) m.p. 37° (lit. (11) m.p. 35.5-37°); nmr: δ ppm 7.37 (d, 1H, H-2), 7.03 (d, 1H, H-3) 3.02 (m, 2H, -CH_2CO), 2.51 (m, 2H, CH_2-CH_2), 2.23 (m, 2H, -CH_2-CH_2-CH_2-CO); ir: ν max 1675 cm^{-1} (C=O).

Table 2

Spectroscopic Data of 7-Substituted Thieno[2,3-*h*][1]benzopyran-8-ones (**9**)

		Nmr (a,b) (δ ppm)					
R^1	R^2	H^1	R^1	H-4	H-5	H-6	Ir (c) (ν max) cm^{-1}
H	CN	8.06 (d)	8.32 (d)	8.36 (d)	7.95 (d)	9.34 (s)	1740 (C=O) 2230 (CN)
H	$CONH_2$	7.85 (d)	8.06 (d)	8.14 (d)	7.94 (d)	9.06 (s)	3400 (NH) 1720 (C=O) 1685 ($CONH_2$)
H	CO_2CH_3	8.03 (d)	8.28 (d)	8.31 (d)	8.07 (d)	9.18 (s)	1755 (C=O) 1695 (CO_2CH_3)
H	$CO_2C_2H_5$	7.98 (d)	8.24 (d)	8.28 (d)	8.04 (d)	9.11 (s)	1745 (C=O) 1690 ($CO_2C_2H_5$)
Br	CN	7.86 (s)	—	7.95 (d)	7.76 (d)	9.10 (s)	2210 (CN) 1725 (C=O)
Br	$CONH_2$	7.86 (s)	—	7.87 (d)	7.87 (d)	8.90 (s)	3380 (NH) 1710 (C=O) 1680 ($CONH_2$)
Br	$CSNH_2$	7.85 (s)	—	7.95 (d)	7.76 (d)	9.10 (s)	3330 (NH) 1700 (C=O)
Br	CO_2CH_3	7.82 (s)	—	7.92 (d)	7.75 (d)	8.78 (s)	1745 (C=O) 1700 (CO_2CH_3)
Br	$CO_2C_2H_5$	7.73 (s)	—	7.94 (d)	7.77 (d)	8.81 (s)	1755 (C=O) 1700 ($CO_2C_2H_5$)
CH_3	CN	7.48 (s)	2.66 (s)	7.96 (d)	9.01 (s)		2220 (CN) 1700 (C=O)
CH_3	$CSNH_2$	7.49 (s)	2.63 (s)	7.96 (d)	7.88 (d)	9.18 (s)	3290 (NH) 1700 (C=O)
CH_3 *	CO_2CH_3	7.39 (s)	2.62 (s)	7.60 (d)	7.34 (d)	8.61 (s)	1755 (C=O) 1700 (CO_2CH_3)
CH_3	$CO_2C_2H_5$	7.38 (s)	2.58 (s)	7.85 (d)	7.65 (d)	8.79 (s)	1750 (C=O) 1700 ($CO_2C_2H_5$)

(a) Spectra recorded in DMSO-d_6. (b) Chemical shifts due to amide and thioamide protons appear as two broad singlets between δ 7-8 ppm and δ 9-10 ppm, respectively. (c) Ir spectra recorded as potassium bromide discs. (*) Nmr spectrum recorded in deuterochloroform.

Table 3 (a)

Analytical Data of *O,O*-Diethyl Thiophosphonohydrazones (**14**)

R^1	R^2	M.p.	Yield (%)	Analysis					
				Calcd.			Found		
				C	H	N	C	H	N
H	H	103°	72	45.3	6.0	8.8	45.4	6.1	8.7
H	Br	122°	77.5	36.3	4.5	7.1	36.3	4.6	7.0
H	CH_3	65.5°	63	47.0	6.3	8.4	46.8	6.4	8.3
H	NO_2	160.5°	92	39.7	5.0	11.6	39.8	5.0	11.6
NO_2	Br	130°	78	32.6	3.9	9.5	32.7	3.9	9.6
NO_2	CH_3	150.5°	66	41.4	5.3	11.1	41.7	5.4	11.0

(a) Crystallised from *n*-hexane.

Table 4

Spectroscopic Data of *O,O*-Diethyl Thisphosphonohydrozones

R^1	R^2	Nmr (a) (δ ppm)					Ir (d) (ν max)
		R^1	R^2	CH_2 (b)	CH_3 (c)	NH	
H	H	6.78 (d)	7.37 (d)	4.15 (m)	1.35 (t)	6.49 (d)	3310
H	Br	7.32 (s)	—	4.13 (m)	1.35 (t)	6.49 (d)	3260
H	CH_3	7.02 (s)	2.40 (s)	4.14 (m)	1.35 (t)	6.46 (d)	3308
H	NO_2	8.16 (s)	—	4.16 (m)	1.37 (t)	6.62 (d)	3310
NO_2	Br	—	—	4.10 (m)	1.35 (t)	6.61 (d)	3285
NO_2	CH_3	—	2.83 (s)	4.10 (m)	1.35 (t)	6.56 (d)	3315

(a) Spectra recorded in deuterochloroform. (b) The signals due to the methylene protons appear as complex multiplets due to the non-equivalence of the two methylene groups each of which is split by the phosphorous atom. (c) The two methyl groups are equivalent in each case. (d) In potassium bromide discs.

Further elution gave 2-acetyl-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)one **1** (R^1 = H, R^2 = $COCH_3$) (0.7 g., 20% of the mixture, 12% overall yield) m.p. 87° (light petroleum); nmr: δ ppm 7.90 (s, 1H, H-3), 3.07 (m, 2H, -C*H*$_2$CO), 2.60 (m, 2H, -CO-C*H*$_2$), 2.52 (s, 3H, -COC*H*$_3$), 2.25 (m, 2H, -CH$_2$-C*H*$_2$-CO); ir: ν max 1675 cm^{-1} (C=O), 1665 cm^{-1} ($COCH_3$).

Anal. Calcd. for $C_{10}H_{10}O_2S$: C, 61.8; H, 5.2. Found: C, 61.7. H, 5.3.

(b) With Trifluoroacetic Anhydride and Polyphosphoric Acid.

Compound **2** (R^1 = R^2 = H) (5 g.) was refluxed with trifluoroacetic anhydride (20 ml.) and polyphosphoric acid (1 ml.) for three hours, after which the reaction mixture was worked up in the same way as described above to give **1** (R^1 = R^2 = H) (0.75 g., 15%).

(c) With Propanoic Anhydride and Polyphosphoric Acid.

Compound **2** (R^1 = R^2 = H) (5 g.) was treated in the same way with propanoic anhydride (25 ml.) and polyphosphoric acid (1 ml.). The usual work-up and vacuum distillation gave **1** (R^1 = R^2 = H), b.p. 92°/1 mm (2 g., 40%). The vacuum distillation was continued to give 2-propionyl-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)one **1** (R^1 = H, R^2 = $COCH_2CH_3$) b.p. 186°/1 mm. (1.6 g., 26.2%). M.p. 77-78° (light petroleum); nmr: δ ppm 7.91 (s, 1H, H-3), 2.8 (q, 2H, CH_2) **1.2 (t, 3H, CH_3)**; ir: ν max. 1670 cm^{-1} ($COCH_2CH_3$).

Anal. Calcd. for $C_{11}H_{12}OS$: C, 63.5; H, 5.8. Found: C, 63.4; H, 5.9.

(d) With Hexanoic Anhydride and Polyphosphoric Acid.

Compound **2** (R^1 = R^2 = H) (5 g.) was similarly treated with hexanoic anhydride (25 ml.) and polyphosphoric acid (1 ml.). After the usual work up and vacuum distillation 2-hexanoyl-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)one **1** (R^1 = H, R^2 = $COCH_2CH_2CH_2CH_2CH_3$) was obtained (2.5 g., 34.2%) b.p. 190°/1 mm, m.p. 41-42° (light petroleum); nmr: δ ppm 7.91 (s, 1H, H-3); ir (neat): ν max 1670 cm^{-1} (C=O) 1650 cm^{-1} ($COCH_2CH_2CH_2CH_2CH_3$).

Anal. Calcd. for $C_{14}H_{18}O_2S$: C, 67.2; H, 7.3. Found: C, 67.2; H, 7.3.

Evaporation of the mother liquor after the 2-hexanoyl derivative was crystallized, gave **1** (R^1 = R^2 = H) (0.01 g.).

Nitration of 6,7-Dihydrobenzo[*b*]thiophen-4(5*H*)one.

Compound **1** (R^1 = R^2 = H) (3 g.) and concentrated sulphuric acid (30 ml.) were cooled to −10° in a three-necked round bottomed flask (250 ml.), equipped with a mechanical stirrer. A mixture of concentrated sulphuric acid (15 ml.) and concentrated nitric acid (d = 1.42) (1.5 ml.) was added over thirty minutes, under vigorous stirring, keeping the temperature of the reaction mixture between −10° and −5°. The stirring was continued for further fifty minutes and the temperature was allowed to rise to 5°, after which period the reaction mixture was poured into crushed ice. The precipitated solid was collected and was washed free of acid with ice-cold water. 2-Nitro-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)one **1** (R^1 = H, R^2 = NO_2) (3.2 g., 82%) was obtained as a pale yellow solid, m.p. 114-115° (light petroleum); nmr: δ ppm 8.1 (s, 1H, H-3); ir: ν max 1690 cm^{-1} (C=O).

Anal. Calcd. for $C_8H_7NO_3S$: C, 48.7; H, 3.6; N, 7.1. Found: C, 48.7; H, 3.6; N, 7.0.

2-Methyl-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)one (23).

Compound **1** (R^1 = H, R^2 = CH_3) was similarly nitrated to give 2-methyl-3-nitro-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)one **1** (R^1 = NO_2, R^2 = CH_3) in 48% yield, m.p. 108-100° (light petroleum); nmr: δ ppm 2.42 (s, 3H, CH_3); ir: ν max 1680 cm^{-1} (C=O).

Anal. Calcd. for $C_9H_9NO_3S$: C, 51.2; H, 4.3; N, 6.6. Found: C, 51.3; H, 4.3; N, 6.5.

Succinoylation of 6,7-Dihydrobenzo[*b*]thiophen-4(5*H*)one.

Succinic anhydride (4.4 g.) was dissolved in boiling dichloromethane (90 ml.). After cooling to room temperature, finely pulverized anhydrous aluminium chloride (11.7 g.) was added in portions to the vigorously stirred solution under anhydrous condition. The stirring was continued for a further fifteen minutes after all the aluminium chloride was added. A solution of **1** (R^1 = R^2 = H) (6.08 g.) in dichloromethane (15 ml.) was added dropwise to the bright red reaction mixture. After the addition was complete, the mixture was stirred for four hours at 20° followed by refluxing for sixty hours. After cooling, it was poured into crushed ice and concentrated hydrochloric acid, the organic layer was separated and the aqueous layer was exctracted with dichloromethane (3 × 100 ml.). The combined organic layer was extracted with 2*M* sodium hydroxide (3 × 100 ml.). On acidification of the alkaline extract, 2-succinoyl-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)one **1** (R^1 = H, R^2 = $-COCH_2CH_2CO_2H$) separated as a brown amorphous solid which was collected and recrystallized from water (decolourizing charcoal) (5.8 g., 58%), m.p. 163-165° dec.; nmr (acetone-d_6): δ ppm 7.97 (s, 1H, H-3). The signals due to all the methylene protons appear as a series of multiplets between δ 2.15 and δ 3.35 ppm ir: ν max 3180 cm^{-1} (br) (OH) 1730 cm^{-1} (CO_2H) 1670 cm^{-1} (C=O ring) 1660 cm^{-1} (C=O side chain).

Anal. Calcd. for $C_{12}H_{12}O_4S$: C, 57.1; H, 4.8. Found: C, 57.0; H, 4.8.

Reduction of the 2-Succinoyl Derivative.

Potassium hydroxide (4 g.) was dissolved in warm diethylene glycol (50 ml.). After the solution was cooled to room temperature, 2-succinoyl-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)one was added to it under stirring followed by hydrazine hydrate (2.2 ml.), over ten minutes. The mixture was stirred and heated at 150° for one hour and at 200° for two hours with continuous removal of the distillate. After cooling, the contents of the flask were poured into crushed ice and acidified with dilute hydrochloric acid. The separated oil was extracted with ether (5 × 100 ml.), and this ether extract was washed with water and dried. The viscous liquid remaining after evaporation of the solvent was vacuum distilled to give γ-(4,5,6,7-tetrahydrobenzo[*b*]thienyl)propionic acid **6**, b.p. 180°/1 mm. (1.4 g., 31.5%) which solidified on cooling as a glass; nmr: δ ppm 11.18 br (s, 1H, CO_2H) (deuterium oxide exchange) 6.41 (s, 1H, H-3); ir: ν max 3060 cm^{-1} (br) (OH), 1700 cm^{-1} (CO_2H).

Anal. Calcd. for $C_{12}H_{16}O_2S$: C, 64.3; H, 7.1. Found: C, 64.5; H, 7.1.

1,2,5,6,7,8-Hexahydrodibenzothiphen-4(3*H*)one **7**.

The above acid (1 g.), acetic anhydride (15 ml.), and polyphosphoric acid (1 ml.) were refluxed for two hours. After working up, the product was extracted with chloroform. The crude product obtained after drying and evaporation of the solvent was steam-distilled to give **7** (0.27 g., 33%) as a white crystalline solid which develops a greenish tinge on standing, m.p. 55°; nmr: spectrum showed a series of complex multiplets between δ 1.7 and δ 3.05 ppm which account for the methylene groups present in the molecule; ir: ν max 1670 cm^{-1} (C=O).

Anal. Calcd. for $C_{12}H_{14}OS$: C, 69.9; H, 6.8. Found: C, 69.9; H, 7.0.

Chlorination of 2-Methyl-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)one.

2-Methyl-6,7-dihydrobenzo[*b*]thiophen (3.32 g.) was dissolved in carbon tetrachloride (150 ml.) and benzoyl peroxide (0.1 g.) was added to the solution which was irradiated with two 200 watt tungsten lamps. Freshly crystallized *N*-chlorosuccimimide (2.66 g.) was added in portions to the solution which was vigorously stirred. After the mixture was refluxed for four hours, the solid was filtered off and the solvent evaporated. The residue was vacuum distilled to give 5-chloro-2-methyl-6,7-dihydrobenzo-[*b*]thiophen-4(5*H*)one **5** b.p. 135-140°/1 mm. which solidified on cooling and was crystallized from light petroleum (2.7 g.; 67%) m.p. 77-79°; nmr: δ ppm 7.05 (s, 1H, H-3) 4.45 (m, 1H, H-5); ir: ν max 1680 cm^{-1} (C=O).

Anal. Calcd. for C_9H_9ClOS: C, 54.0; H, 4.5. Found: C, 54.1; H, 4.6.

General Method for the Preparation of 7-Substituted Thieno[2,3-*h*][1]-benzopyran-8-ones **9**.

The 4-hydroxybenzo[*b*]thiophen-5-carbaldehydes **4** were prepared following the methods of Sy (9) and Cagniant (10). Two members of the series *viz.*, 2-methyl and the 2-bromo derivatives have not been hitherto reported in the literature.

2-Methyl-4-hydroxybenzo[*b*]thiophen-5-carbaldehyde **4** (R = CH_3).

This compound was obtained in 84% yield, and was purified by steam-distillation, m.p. 68°; nmr: δ ppm 11.88 br (s, 1H, OH) (deuterium oxide exchange) 9.88 (s, 1H, CHO) 2.58 (s, 1H, CH_3). The signals due to H-3, H-7 and H-8 appear between δ 7.25 and δ 7.30; ir: ν max 3450 cm^{-1} br (OH), 1645 (cm^{-1} (CHO).

Anal. Calcd. for $C_9H_{10}OS$: C, 62.5; H, 4.2. Found: C, 62.7; H, 4.3.

2-Bromo-4-hydroxybenzo[*b*]thiophen-5-carbaldehyde, **4** (R = Br).

This compound was obtained in 85% yield, m.p. 119°; nmr: δ ppm 11.89 br (s, 1H, OH) (deuterium oxide exchange) 9.88 (s, 1H, CHO) 7.56 (s, 1H, H-3). The signals due to H-7 and H-8 appear as an AB quartet centred at δ 7.3; ir: ν max 3420 cm^{-1} br (OH), 1660 cm^{-1} (CHO).

Anal. Calcd. for $C_9H_5BrO_2S$: C, 42.0; H, 2.0. Found: C, 42.4; H, 2.1.

The appropriate hydroxy aldehyde (0.01 mole) and the cyanomethylene compound (0.01 mole) were suspended in absolute ethanol (50 ml.) and a few drops of triethylamine were added. After shaking for thirty minutes at room temperature and leaving it to stand until no further precipitation was apparent, the crude imine **8** was collected and washed with ethanol. It was immediately hydrolyzed to **9** by heating on a boiling water bath with 30 to 40 ml. of dilute hydrochloric acid. The crude product was collected and purified by recrystallization.

3-Methyl-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)one **1** (R^1 = CH_3, R^2 = H).

γ-(4-Methyl-2-thienyl)butyric acid (15) **2** (R^1 = CH_3, R^2 = H) (3 g.) was heated with acetic anhydride (25 ml.) and polyphosphoric acid (1 ml.) at 36° for three hours. On working up, 2 g. of crude product was obtained which was chromatographed on silica gel. Elution with a mixture of light petroleum and ethyl acetate (6:4) afforded 3-methyl-6,7-dihydrobenzo[*b*]-thiophen-4(5*H*)one (0.15 g., 7.5% of the mixture) m.p. 27-28° (light petroleum); nmr: δ ppm 6.6 (s, 1H, H-2), 2.42 (s, 3H, H-3); ir (neat): ν max 1675 cm^{-1} (C=O).

Anal. Calcd. for $C_9H_{10}OS$: C, 65.0; H, 6.0. Found: C, 64.8; H, 6.2.

Further elution gave 3-methyl-2-acetyl-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)one (15) (1.5 g., 75% of the mixture).

Reaction of 2-Bromo-3-nitro-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)one with Methyl Thioglycollate.

Sodium (0.23 g.) was dissolved in absolute methanol (20 ml.) and methyl thioglycollate (0.53 g.) in absolute methanol (30 ml.) was added dropwise. After stirring for an hour at room temperature, under anhydrous condition, a solution of 2-bromo-3-nitro-6,7-dihydrobenzo[*b*]-thiophen-4(5*H*)one (1.38 g.) in absolute methanol (70 ml.) was added dropwise. After further stirring for ninety minutes, the solvent was removed under reduced pressure and the residue vacuum distilled to give **1** (R^1 = H, R^2 = $SCH_2CO_2CH_3$) as a glass b.p. 170°/1 mm. (1.2 g., 80%), R_f = 0.13 (light petroleum:ethyl acetate, 7:3); nmr: δ ppm 3.74 (CO_2CH_3), 3.62 (s, CH_2); ir (neat): ν max 1745 cm^{-1} (CO_2CH_3) 1680 cm^{-1} (C=O).

Anal. Calcd. for $C_{11}H_{11}NO_5S_2$: C, 46.9; H, 3.9; N, 4.9. Found: C, 47.1; H, 3.7; N, 4.6.

General Method for the Preparation of *O,O*-Diethyl Thiophosphonohydrazones **14**.

O,O-Diethyl thiophosphonohydrazine (21,22) (0.05 mole) and the appropriate ketone (0.05 mole) were refluxed in absolute ethanol for five hours. The residue left after evaporation of the solvent was purified by recrystallization to give the desired compound.

Acknowledgements.

We wish to thank Drs. A. C. Knipe, R. M. Scrowston and W. E. Watts for helpful discussions. We are also grateful to Messrs. Croda Synthetic

Chemicals (Four Ashes nr. Wolverhamptom, West Midlands) for a generous gift of chemicals. One of us (H.J.) thanks University of Wales for a research studentship.

REFERENCES AND NOTES

(1) B. Iddon and R. M. Scrowston in "Advances in Heterocyclic Chemistry", A. R. Katritzky, Ed., Academic Press London, Vol. 11, 1970, p. 253.

(2) K. Clarke, R. M. Scrowston and T. M. Sutton, *J. Chem. Soc.,Perkin Trans. I,* 1196 (1973).

(3) A. Mustafa, "Furopyrans and Furopyrones", Academic Press, London.

(4) A. Mustafa, S. M. A. D. Zayed and A. Emran, *Ann. Chem.,* **704**, 176 (1967).

(5) P. M. Chakrabarti, N. B. Chapman and K. Clarke, *J. Chem. Soc. C,* 1 (1969).

(6) A. K. Bose, H. Fujiwara, V. S. Kamat, G. K. Trivedi and S. C. Bhattachayya, *Tetrahedron,* **35**, 13 (1979).

(7) M. H. A. Elgamal, N. H. Elewa, E. A. M. Elkhrisy and H. Duddeck, *Phytochemistry,* **18**, 139 (1979).

(8) J. S. A. Brunskill, A. De, Z. Elagbar, D. F. Ewing and H. Jeffrey, *Synth. Commun.* **8**, 533 (1978).

(9) M. Maillet and M. Sy, *Compt. Rend.,* **266C**, 1545 (1968).

(10) P. Caginant and G. Kirsch, *ibid.,* **281C**, 393 (1975).

(11) L. F. Fieser and R. G. Kennelly, *J. Am. Chem. Soc.,* **57**, 1611 (1935).

(12) S. Nishimura, M. Nakamura, M. Suzuki and E. Imoto, *Nippon Kagaku Zasshi,* **83**, 343 (1962); *Chem. Abstr.,* **59**, 3862 (1963).

(13) G. Baddeley and D. Voss, *J. Chem. Soc.,* 418 (1954).

(14) Dr. R. M. Scrowston (University of Hull) has lately informed us through a personal communication, that on one instance he had noticed the formation of 2-acetyl-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)one.

(15) N. B. Chapman, R. M. Scrowston and T. M. Sutton, *J. Chem. Soc., Perkin, Trans. I,* 3011 (1972).

(16) D. T. Drewry and R. M. Scrowston, *J. Chem. Soc. C,* 2750 (1969).

(17) S. Gronowitz in "Advances in Heterocyclic Chemistry", Vol. 1, A. R. Katritzky, Ed., Academic Press, London, 1963, p. 56.

(18) P. Caginant and Mme. P. Caginant, *Bull. Soc. Chim. France,* 336 (1952).

(19) A. E. S. Fairfull, J. L. Lowe and D. A. Peak, *J. Chem. Soc.,* 742 (1952).

(20) Mobil Oil Corporation, British Patent, 1,097,634 (1968); *Chem. Abstr.,* **69**, 10353f (1968).

(21) A. Krutosikova, V. Konecry and J. Kovac, *Collect. Czech. Chem. Commun.,* **43**, 2643 (1978).

(22) H. Tolkmith, *J. Am. Chem. Soc.,* **84**, 2097 (1962).

(23) N. P. Buu-Hoï, N. Hoán and N. Khôi, *Rec. Trav. Chim.,* **69**, 1053 (1950).