Thiophen Derivatives. Part XX.[1] Further Studies on the Elbs Reaction of Aroylbenzo[*b*]thiophens

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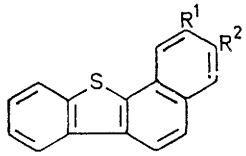
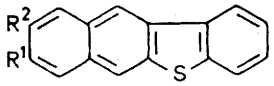
3-(4-Methoxy-2-methylbenzoyl)- and 3-(4-methoxy-2,5-dimethylbenzoyl)-benzo[*b*]thiophen underwent the Elbs reaction with rearrangement to give derivatives of benzo[*b*]naphtho[2,1-*d*]thiophen, whereas 2-(4-methoxy-2,5-dimethylbenzoyl)benzo[*b*]thiophen gave the normal cyclisation product, *i.e.* a benzo[*b*]naphtho[2,3-*d*]-thiophen.

BADGER and CHRISTIE [2] reported that 3-*o*-toluoylbenzo[*b*]thiophen undergoes Elbs pyrolysis to give benzo[*b*]naphtho[2,1-*d*]thiophen (I) through a novel rearrangement,[2] and two of us recently confirmed this;[3] earlier, however, Werner [4] had found that the Elbs



(I; $R^1 = R^2 = H$)
(II; $R^1 = H$, $R^2 = OMe$)
(III; $R^1 = Me$, $R^2 = OMe$)



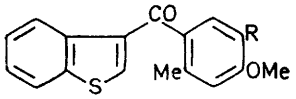
(IV; $R^1 = R^2 = H$)
(V; $R^1 = Me$, $R^2 = OMe$)

cyclisation of 2-benzoyl-3-methylbenzo[*b*]thiophen proceeded normally, giving benzo[*b*]naphtho[2,3-*d*]thiophen (IV). In view of this contrasting behaviour of the two isomeric benzo[*b*]thiophen ketones, it was interesting to examine more extensively the scope and limitations of this rearrangement, with several diversely substituted aroylbenzo[*b*]thiophens, especially as some 3-aroylbenzo[*b*]thiophens cyclise normally.[2,5,6] Furthermore, the formal resemblance of benzo[*b*]naphtho[2,1-*d*]-thiophen (I) to the carcinogenic and enzyme-inducing hydrocarbon chrysene suggested that derivatives of (I) might have similar activity.[7]

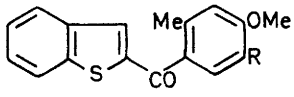
Friedel–Crafts acylation of benzo[*b*]thiophen with 4-methoxy-2-methyl- and 4-methoxy-2,5-dimethylbenzoyl chloride, with aluminium chloride as catalyst and methylene chloride as solvent, afforded, as expected from earlier observations,[8] mixtures of the 2- and 3-aroyl compounds, which could be separated into their components; the structures of these ketones were readily determined by analysis of their n.m.r. spectra,

[1] Part XIX, N. P. Buu-Hoï, M. Mangane, M. Renson, and L. Christiaens, *J. Chem. Soc.* (*B*), 1969, 971.
[2] G. M. Badger and B. J. Christie, *J. Chem. Soc.*, 1956, 3435.
[3] N. P. Buu-Hoï, A. Croisy, and P. Jacquignon, *J. Chem. Soc.* (*C*), 1969, 339.
[4] E. G. G. Werner, *Rec. trav. Chim.*, 1949, **68**, 520.
[5] P. Faller, *Bull. Soc. chim. France*, 1966, 3618; 3667; *Compt. rend.*, 1961, **252**, 1034; 1964, **258**, 2839; 1965, **260**, 3686; 1966, **262**, *C*, 581.
[6] See also the comprehensive review on the benzo[*b*]thiophens: B. Iddon and R. M. Scrowston, *Adv. Heterocyclic Chem.*, 1970, **11**, 177.
[7] *Cf.* N. P. Buu-Hoï, D.-P. Hien, and Ph. Mabille, in Japanese Cancer Association Gann Monograph 2: Cancer Chemotherapy, Maruzen Co. Ltd., Tokyo, 1967, p. 71; N. P. Buu-Hoï and D.-P. Hien, *Biochem. Pharmacol.*, 1968, **17**, 1227; 1969, **18**, 741.
[8] N. P. Buu-Hoï and P. Cagniant, *Rec. trav. Chim.*, 1948, **67**, 64; M. W. Farrar and R. Levine, *J. Amer. Chem. Soc.*, 1950, **72**, 4433; further literature in ref. 6.

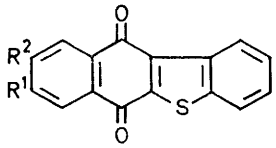
taking into account Faller's observations on the differences in the spectra of other isomeric 2- and 3-aroylbenzo[*b*]thiophens.[9] The features of the spectra of



(VI; R = H)
(VII; R = Me)



(VIII; R = H)
(IX; R = Me)



(X; R^1 = OMe, R^2 = H)
(XI; R^1 = Me, R^2 = OMe)

ketones (VI)—(IX) (taken in $CDCl_3$; internal reference $SiMe_4$) are listed in Table 1; the chemical shifts for the 2- and 3-protons observed are entirely consistent with Faller's observations.

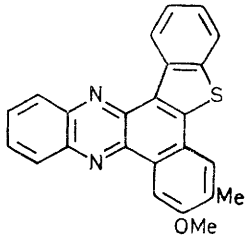
TABLE 1

N.m.r. spectra: chemical shifts * in p.p.m.

Ketone (VI)		Ketone (VIII)	
Signal	Proton	Signal	Proton
8·6br (m) †	4-H	7·8br (m)	4- and 7-H
7·82 (m)	7-H	7·63 (s)	3-H
7·8 (s)	2-H	7·35br (m)	5-, 6-, and 6′-H
7·4 (m)	5-, 6-, and 6′-H	6·8 (m)	3′-H
6·78 (s) ‡	3′-H	6·75 (q)	5′-H
6·7 (q) ‡	5′-H	3·82 (s)	OMe
3·78 (s)	OMe	2·45 (s)	Me
2·4 (s)	Me		
Ketone (VII)		**Ketone (IX)**	
8·65br (m) †	4-H	7·82br (m)	4- and 7-H
7·87br (m)	7-H	7·65 (s)	3-H
7·85 (s)	2-H	7·38br (m)	5-, 6-, and 6′-H
7·43br (m)	5- and 6-H	6·73 (s)	3′-H
7·25 (s) ‡	6′-H	3·86 (s)	OMe
6·72 (s) ‡	3′-H	2·45 (s)	2′-Me
3·85 (s)	OMe	2·21 (s)	5′-Me
2·42 (s)	2′-Me		
2·18 (s)	5′-Me		

* Centre values, except for singlets. † Deshielded. ‡ Shielded.

Pyrolysis of ketone (VII) afforded a complex mixture which could be resolved by chromatography on silica into 3-methoxy-2-methylbenzo[*b*]naphtho[2,1-*d*]thiophen (III), the structure of which was established by oxidation with chromic acid to the corresponding *ortho*-quinone, which with *o*-phenylenediamine, gave the phenazine (XII). The structure assigned to (III) was



(XII)

further confirmed by its n.m.r. spectrum (in CCl_4) (Figure 1). Pyrolysis of ketone (IX), on the other hand, occurred, in line with Werner's observation,[4] without rearrangement, and led to 9-methoxy-8-methylbenzo[*b*]naphtho[2,3-*d*]thiophen (V), the n.m.r. spectrum ($CDCl_3$) of which is wholly consistent with the assigned structure (Figure 2; note the two singlets at δ 8·1 and 8·47 p.p.m. characteristic of the *meso*-protons 6- and

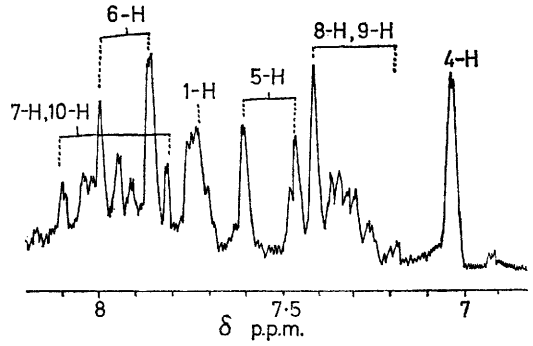


FIGURE 1 N.m.r. spectrum of compound (III) in carbon tetrachloride

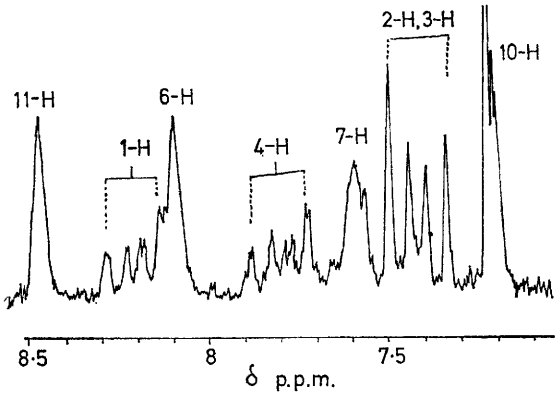


FIGURE 2 N.m.r. spectrum of compound (V) in deuteriochloroform

11-H respectively). In addition to compound (V), large amounts of 9-methoxy-8-methylbenzo[*b*]naphtho[2,3-*d*]thiophen-6,11-quinone (XI) were isolated; this quinone, which we also prepared by oxidation of (V) with chromic acid, was clearly an artefact due to the purification of the crude product by chromatography on alumina, which promotes oxidation.[2] When silica was used in place of alumina this quinone was not isolated.

As expected from these findings, ketone (VI) underwent Elbs pyrolysis with rearrangement, the main product showing properties very similar to those of (III) and an n.m.r. spectrum consistent with the 3-methoxybenzo[*b*]naphtho[2,1-*d*]thiophen structure (II). However, a minor product, 8-methoxybenzo[*b*]naphtho[2,3-*d*]thiophen-6,11-quinone (X) was obtained, whose structure was established by elemental analysis, and by its inability to react with *o*-phenylenediamine; the structure (X) is fully consistent with its n.m.r. spectrum

[9] P. Faller, *Bull. Soc. chim. France*, 1949, 934.

(in $CDCl_3$) (Figure 3) which shows, in particular, the deshielding effect of the carbonyl groups on 1-, 10-, and 7-H (the shielding effect exerted by the methoxy-group

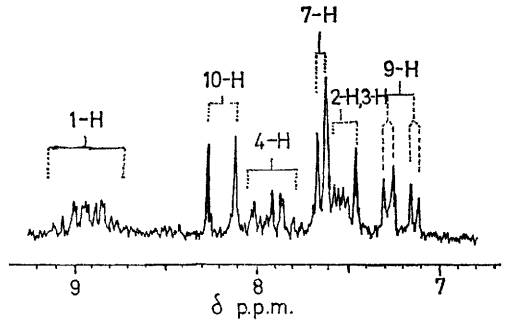


FIGURE 3 N.m.r. spectrum of compound (X) in deuteriochloroform

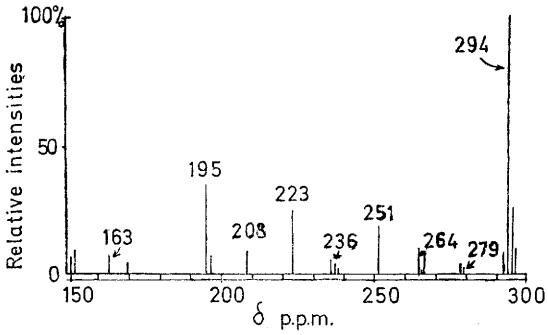
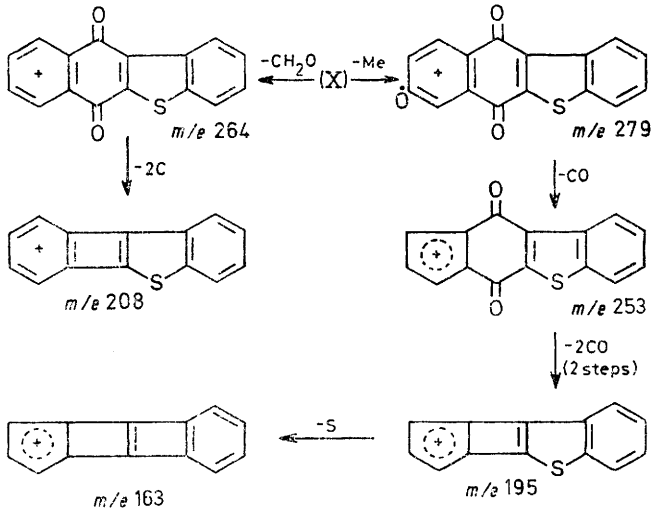


FIGURE 4 Mass spectrum of compound (X)

TABLE 2

Main fragmentation ions from (X)



on 7-H thus being overcome in part). Also consistent with structure (X) is its mass spectrum (Figure 4), with a fragmentation pattern (Table 2) which is in conformity with the behaviour expected of an anthraquinone [10] possessing in addition an ether function.[11] The presence of the linear quinone (X) [which, like (XI), was formed by oxidation during chromatography on alumina] alongside the angular compound (II) supports Badger and Christie's suggestion [2] that the rearrangement which occurs during the thermocyclisation of 3-aroylbenzo[*b*]thiophens (and which our work shows is frequently observed in such ketones) might involve a linear, oxidisable intermediate [which is not the linear dehydration product, as in the present work we found that compound (V) did not undergo thermal rearrangement].

Pyrolysis of ketone (VIII) afforded resinous compounds from which no pure substance could be isolated.

EXPERIMENTAL

Preparation of Intermediates.—4-Methoxy-2-methylbenzoic acid,[12] m.p. 177° (from methanol) was prepared in 70% yield by oxidation for 6 h of 4′-methoxy-2′-methylacetophenone (98·5 g) in dioxan (100 ml) with cold aqueous sodium hypobromite [from bromine (105 ml) and sodium hydroxide (194 g) in water (1200 ml)]; 4-methoxy-2,5-dimethylbenzoic acid,[13] m.p. 168° (from methanol), was similarly prepared from 4-methoxy-2′,5′-dimethylacetophenone (70% yield). 4-Methoxy-2-methylbenzoyl chloride, m.p. 53° (from hexane), b.p. 145° at 12 mmHg (Found: C, 58·2; H, 5·0; Cl, 19·4. $C_9H_9ClO_2$ requires C, 58·4; H, 4·9; Cl, 19·2%) and *4-methoxy-2,5-dimethylbenzoyl chloride*, m.p. 90° (from hexane), b.p. 167° at 22 mmHg (Found: C, 60·4; H, 5·5; Cl, 17·8. $C_{10}H_{11}ClO_2$ requires C, 60·5; H, 5·5; Cl, 17·9%) were prepared in 95% yield from the reaction of the corresponding acids with thionyl chloride in benzene.

Reaction of 4-Methoxy-2-methylbenzoyl Chloride with Benzo[b]*thiophen.*—To a stirred solution of benzo[*b*]thiophen (13·5 g) and 4-methoxy-2-methylbenzoyl chloride (22·5 g) in methylene chloride (250 ml), aluminium chloride (20 g) was added in small portions during 1 h at 220°. After 5 h, the mixture was decomposed with ice–hydrochloric acid, and the organic layer was washed with 5% aqueous sodium hydroxide and with water, dried (Na_2SO_4), the solvent was distilled off, and the residue was fractionated *in vacuo*. The portion with b.p. 150—235° at 0·05 mmHg afforded, on fractional crystallisation from cyclohexane then from ethanol, *3-(4-methoxy-2-methylbenzoyl)benzo*[b]*thiophen* (VI) (5·6 g), as prisms, m.p. 99° (Found: C, 72·0; H, 5·3. $C_{17}H_{14}O_2S$ requires C, 72·3; H, 5·0%) and *2-(4-methoxy-2-methylbenzoyl)benzo*[b]*thiophen* (VIII) (4·8 g), as prisms, m.p. 121° (Found: C, 72·1; H, 5·1%). Gas chromatography showed that no other isomer was present in the crude product.

Reaction of 4-Methoxy-2,5-dimethylbenzoyl Chloride with Benzo[b]*thiophen.*—The Friedel–Crafts reaction, performed as just described, afforded after usual treatment of the product (b.p. 200—260° at 0·05 mmHg) *3-(4-methoxy-2,5-dimethylbenzoyl)benzo*[b]*thiophen* (VII) (16%), as prisms, m.p. 142° (from cyclohexane) (Found: C, 73·0; H, 5·3. $C_{18}H_{16}O_2S$ requires C, 73·0; H, 5·4%) and *2-(4-methoxy-2,5-dimethylbenzoyl)benzo*[b]*thiophen* (IX) (14%), as silky

[10] G. Spiteller and M. Spiteller-Friedmann, *Monatsh.*, 1963, **93**, 1395.

[11] J. H. Beynon, 'Mass Spectrometry and its Applications to Organic Chemistry,' Elsevier, Amsterdam, 1960, p. 397.

[12] Prepared differently by C. Schall, *Ber.*, 1879, **12**, 825.

[13] Prepared differently by G. R. Clemo, R. D. Haworth, and E. Walton, *J. Chem. Soc.*, 1929, 2376.

needles, m.p. 131° (Found: C, 73·0; H, 5·1%). Substantially higher yields (27% for the 3-isomer and 13·5% for the 2-isomer) were obtained when aluminium chloride was replaced by tin(IV) chloride.

Pyrolysis of Ketone (VII).—When this compound (4·1 g) was heated at 380—390° for 2 h under nitrogen a resinous product was obtained which was treated with benzene; an insoluble residue (0·8 g) was left, and chromatography of the benzene solution on a silica column, and elution of the middle layer with benzene–cyclohexane (1 : 1), afforded 3-*methoxy*-2-*methylbenzo*[b]*naphtho*[2,1-d]*thiophen* (III), as pale yellow leaflets, m.p. 176°, (0·75 g) (from hexane) (Found: C, 77·5; H, 5·0; S, 11·3. $C_{18}H_{14}OS$ requires C, 77·7; H, 5·1; S, 11·5%). No other cyclisation product was observed; oxidation of compound (III) with chromic acid in boiling acetic acid furnished a yellow quinone (90% yield) whose solution in boiling ethanol gave, with *o*-phenylenediamine, 8-*methoxy*-7-*methylbenzo*[a][1]*benzothieno*[2,3-c]*phenazine* (XII) in theoretical yield as pale yellow leaflets, m.p. 272° (from acetic acid) (Found: N, 7·3%; *M*, 380. $C_{24}H_{16}N_2OS$ requires N, 7·4%; *M*, 380·3).

Pyrolysis of Ketone (IX).—This ketone (3 g) was heated as already described at 350—370° for 180 min; chromatography on alumina of a solution of the pyrolysate in benzene (insoluble residue: 0·7 g) gave, on elution with benzene containing 0·5% ethanol, 9-*methoxy*-8-*methylbenzo*[b]*naphtho*[2,3-d]*thiophen* (V), as cream, sublimable leaflets (0·1 g), m.p. 206° (from cyclohexane) (Found: C, 77·6; H, 5·3. $C_{18}H_{14}OS$ requires C, 77·7; H, 5·1%); this compound was thermally stable and was recovered unchanged after being heated at 370° under nitrogen, and 9-*methoxy*-8-*methylbenzo*[b]*naphtho*[2,3-d]*thiophen*-6,11-*quinone* (XI), as orange, sublimable needles (0·3 g), m.p. 270° (from cyclohexane–benzene), which gave a dark violet solution in sulphuric acid (Found: C, 70·1; H, 4·0. $C_{18}H_{12}O_3S$ requires C, 70·1; H, 3·9%). The same quinone was obtained when a solution of (V) in acetic acid was heated under reflux with chromic acid until the solution turned green, followed by dilution with water and recrystallisation of the precipitate.

Pyrolysis of Ketone (VI).—This was effected as already described (2·7 g) and afforded, after chromatography on alumina of the crude pyrolysate and elution with cyclohexane–benzene (1 : 1), 3-*methoxybenzo*[b]*naphtho*[2,1-d]-*thiophen* (II), as colourless leaflets (0·15 g), m.p. 171° (from propanol) (Found: C, 77·0; H, 4·5; S, 12·1. $C_{17}H_{12}OS$ requires C, 77·3; H, 4·6; S, 12·1%); δ 8·0 and 8·1 (deshielded 6- and 7-H respectively, by analogy with 1- and 9-H in dibenzothiophen [14]), 7·75 (10-H by analogy with 4- and 6-H in dibenzothiophen), 6·95—7·45 (2-, 4-, 8-, and 9-H), and 7·6 and 7·9 (5-H and 1-H, or *vice versa*) p.p.m., and 8-*methoxybenzo*[b]*naphtho*[2,3-d]*thiophen*-6,11-*quinone* (X), as orange microprisms (0·02 g), m.p. 217° (from benzene), which gave dark green solutions in sulphuric acid (Found: C, 69·1; H, 3·6; S, 10·9. $C_{17}H_{10}O_3S$ requires C, 69·4; H, 3·4; S, 10·9%).

Pyrolysis of ketone (VIII) (2·75 g) gave only an intractable resin, in addition to charred, benzene-insoluble material (1·8 g).

The n.m.r. spectra were determined with a Varian A-60 spectrometer, and the mass spectra with an MS-9 apparatus (70 eV; temperature of insertion, 200°). For these measurements we thank the Departments of N.M.R. (Mrs. L. Alais) and Mass Spectrometry (Dr. B. Das) of this Institute.

[0/583 *Received, April 14th,* 1970]

[14] B. Clin and B. Lemanceau, *J. Chim. phys.* 1969, 1327.