9. *Oxygen Heterocycles. Part IX.* The Elbs Reaction in the Dibenzofuran Series.*

By Ng. Ph. Buu-Hoï and Denise Lavit.

The Elbs reaction of 2-*o*-toluoyldibenzofuran is shown to give a mixture of naphtho(2′ : 3′-1 : 2)- and naphtho(2′ : 3′-2 : 3)-dibenzofuran. 2-(2-Methyl-1-naphthoyl)dibenzofuran undergoes the same reaction, to give also a mixture of the two possible phenanthrodibenzofurans, whose properties have been investigated.

Whereas many nitrogen- and sulphur-containing heterocyclic analogues of condensed carcinogenic hydrocarbons have already been tested for tumour- and/or growth-inhibitory activity,[1] similar oxygen-heterocycles have rarely been investigated. A convenient approach to condensed molecules of this type was Elbs pyrolysis of suitable oxygen-heterocyclic ketones. The choice of ketones with favourable structures was limited to those whose carbonyl group is not directly attached to the furan ring, in view of Badger and Christie's failure [2] to obtain a phenanthrofuran from 2 : 5-dimethyl-3-(2-naphthoyl)-furan because of resinification of the latter. Pyrolysis of 2-*o*-toluoyl- (I) and 2-(2-methyl-1-naphthoyl)-dibenzofuran (II) was therefore investigated. These ketones were obtained isomer-free by Friedel–Crafts acylation of dibenzofuran with *o*-toluoyl chloride and 2-methyl-1-naphthoyl chloride.[3]

Ketone (I) readily underwent the Elbs reaction, to give a mixture of two crystalline

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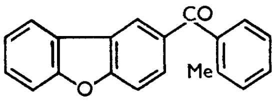
* Part VIII, Buu-Hoï, Saint-Ruf, Loc, and Xuong, *J.*, 1957, 2593.

[1] Cf. Lacassagne, Buu-Hoï, Daudel, and Zajdela, " Advances in Cancer Research," Academic Press, New York, 1956, Vol. IV.

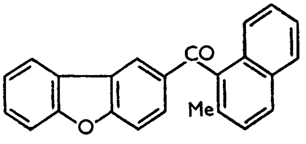
[2] Badger and Christie, *J.*, 1956, 3435.

[3] Cf. Galewsky, *Annalen*, 1891, **264**, 189; Borsche and Bothe, *Ber.*, 1908, **41**, 1843; Mosettig and Robinson, *J. Amer. Chem. Soc.*, 1935, **57**, 2186; Buu-Hoï and Royer, *Rec. Trav. chim.*, 1948, **67**, 175.

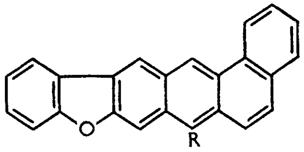
products, one of which was assigned the linear structure of naphtho(2′ : 3′-2 : 3)dibenzofuran (III) on account of its high m. p. (322°) and pronounced yellow colour; the isomeric naphtho(2′ : 3′-1 : 2)dibenzofuran (IV), which, because of its greater solubility in hydrocarbons, could easily be separated from (III), had a considerably lower m. p. (173°) and was only pale yellow. The yield of the linear compound was appreciably the lower, which shows that the known tendency of Elbs reactions to favour the angular structures[4] also applies to oxygen-heterocyclic molecules.



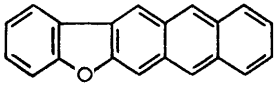
(I)



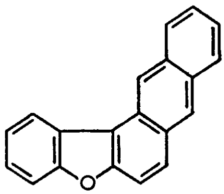
(II)



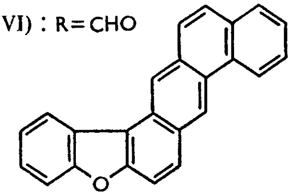
(V) : R=H
(VI) : R=CHO



(III)

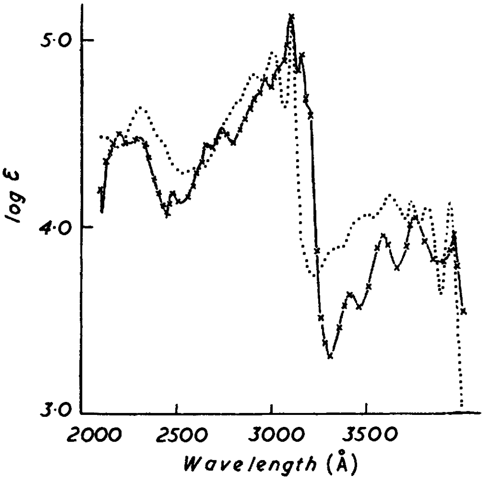


(IV)



(VII)

The pyrolysis of ketone (II) unexpectedly gave only a low yield, of two isomeric yellow compounds. Although there was less marked difference in colour than between compounds (III) and (IV), ultraviolet absorption measurements (see Figure) suggested that the more absorbing isomer (m. p. 247°) was phenanthro(3′ : 2′-2 : 3)dibenzofuran (V), the other compound then being phenanthro(2′ : 3′-1 : 2)dibenzofuran (VII). Chemical support for these assignments lay in the differing behaviour of the two isomers on formylation with *N*-methylformanilide in presence of phosphorus oxychloride. Compound (V), which possesses a reactive *meso*-position, gave an aldehyde (VI), whilst the isomer (VII), whose *meso*-anthracenic positions are both sterically hindered, failed to react. This accords with



· · · *Compound* (VII). —— *Compound* (V).

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[4] Cf. Cook, *J.*, 1931, 487; 1932, 1472.

the fact that of the two *meso*-anthracene positions in benz[*a*]anthracene only the sterically unencumbered position 7 can be formylated.[5]

If the Elbs reaction of 2-(2-methyl-1-naphthoyl)dibenzofuran was for only a short time, a third product was isolated, which was richer in oxygen than compounds (V) and (VII) and was probably an anthrone-like derivative.

The two phenanthrodibenzofurans (V) and (VII) can be considered as benz[*a*]-anthracenes substituted in positions 8 and 9 (Ring Index numbering), both of which are known to be significant for carcinogenic activity,[6] and these two compounds are under biological test in this Institute.

EXPERIMENTAL

2-o-*Toluoyldibenzofuran* (I).—To a solution of dibenzofuran (10 g.) and *o*-toluoyl chloride (18 g.) in anhydrous carbon disulphide (75 c.c.), finely powdered aluminium chloride (9 g.) was added in small portions with stirring, and the mixture left for 3 days at room temperature. After decomposition with ice and hydrochloric acid, the product was taken up in chloroform, the chloroform solution was washed with 5% aqueous sodium hydroxide, then with water, and dried (Na_2SO_4), the solvent removed, and the residue fractionated *in vacuo*. The *ketone*, b. p. 267°/12 mm., crystallised as prisms (13·5 g.), m. p. 100° (from ethanol), giving a yellow halochromy with sulphuric acid (Found: C, 83·8; H, 5·1. $C_{20}H_{14}O_2$ requires C, 83·9; H, 4·9%). Acidification of the alkaline liquors yielded 8 g. of *o*-toluic acid.

Pyrolysis of Ketone (I).—The foregoing ketone (13 g.) was gently refluxed for 1 hr. at atmospheric pressure, with removal of water, and the product was then distilled *in vacuo*, yielding an orange-yellow resin (10 g.), which was taken up in boiling toluene (400 c.c.). The yellow precipitate formed on cooling recrystallised from toluene, giving *naphtho*(2′ : 3′-2 : 3)-*dibenzofuran* (III), yellow leaflets (1·8 g.), m. p. 322°, the halochromy with sulphuric acid being orange, rapidly becoming brown (Found: C, 89·2; H, 4·5. $C_{20}H_{12}O$ requires C, 89·5; H, 4·5%). The toluene mother-liquors yielded, after concentration, a pale yellow precipitate (4·2 g.) which, on repeated crystallisation from *cyclo*hexane, furnished *naphtho*(2′ : 3′-1 : 2)*dibenzofuran* (IV), pale yellow needles (3 g.), m. p. 173°, with halochromy in sulphuric acid the same as for the isomer (Found: C, 89·4; H, 4·6%).

2-(2-*Methyl*-1-*naphthoyl*)*dibenzofuran* (II).—2-Methyl-1-naphthoic acid was prepared by carboxylation of 2-methyl-1-naphthylmagnesium bromide. To a solution of 2-methyl-1-naphthoyl chloride (54 g.) and dibenzofuran (20 g.) in dry carbon disulphide (150 c.c.), aluminium chloride (17·5 g.) was added portionwise, and the mixture left for 3 days, then worked up as for compound (I). The portion boiling at 260—270°/0·5 mm. crystallised as prisms (20·5 g.), m. p. 160°, from ethanol, and gave an orange-yellow halochromy with sulphuric acid (Found: C, 85·5; H, 5·0. $C_{24}H_{16}O_2$ requires C, 85·7; H, 4·8%).

Pyrolysis of Ketone (II).—(*a*) The foregoing ketone (10 g.) was gently refluxed for 1 hr.; the product was distilled *in vacuo*, and taken up in benzene, giving a less-soluble portion which crystallised from benzene to furnish *phenanthro*(3′ : 2′-2 : 3)*dibenzofuran* (V), bright yellow leaflets (0·6 g.), m. p. 247°, giving no colour in cold sulphuric acid but on heating a blue halochromy which rapidly changed to greenish-brown (Found: C, 90·2; H, 4·4. $C_{24}H_{14}O$ requires C, 90·5; H, 4·4%). The benzene mother-liquors gave, on concentration, *phenanthro*-(2′ : 3′-1 : 2)*dibenzofuran* (VII), colourless needles (0·3 g.), m. p. 227° (from ethanol–benzene), giving with hot sulphuric acid a reddish halochromy rapidly becoming greenish-brown (Found: C, 90·2; H, 4·4%). This compound gave from benzene an orange-red picrate, which decomposed on recrystallisation from ethanol or when heated above 150°.

(*b*) Pyrolysis of the ketone (II) (10 g.), when effected in 20 min., yielded, in addition to compounds (V) (0·2 g.) and (VII) (0·1 g.), a *substance*, crystallising as pale yellow needles (0·5 g.), m. p. 241° (decomp. >230°) (from benzene), giving a deep yellow halochromy with sulphuric acid (Found: C, 85·7; H, 4·7. $C_{24}H_{16}O_2$ requires C, 85·7; H, 4·8%). This compound, for which the analytical results suggest the structure of a dihydroanthrone, was not detected in the first pyrolysis experiment.

Formylation of Phenanthro(3′ : 2′-2 : 3)*dibenzofuran* (V).—A mixture of compound (V) (0·57 g.), *N*-methylformanilide (0·36 g.), phosphorus oxychloride (0·38 g.), and dry *o*-dichlorobenzene

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[5] Fieser and Hartwell, *J. Amer. Chem. Soc.*, 1938, **60**, 2555.

[6] Cook, *J.*, 1931, 499, 2529.

(10 c.c.) was heated for 7 hr. on a boiling-water bath. After cooling and filtration, the filtrate was treated with saturated aqueous sodium acetate (10 c.c.), and the solvent and *N*-methylaniline were removed by steam-distillation. The yellow solid residue was filtered off, washed with water, dried, and recrystallised several times from benzene to give, along with unchanged material, a small quantity of *1′-formylphenanthro*(3′ : 2′-2 : 3)*dibenzofuran* (VI), yellow needles (12 mg.), m. p. 255° (Found: C, 86·4; H, 4·1. $C_{25}H_{14}O_2$ requires C, 86·7; H, 4·1%), giving a deep violet halochromy with sulphuric acid. The same formylation, attempted with phenanthro(2′ : 3′-1 : 2)dibenzofuran (VII), resulted only in recovered material, m. p. 227°. The sluggish reactivity of compound (V) and the complete inertia of compound (VII) towards formylation are characteristic of condensed dibenzofurans.[7]

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[7] Buu-Hoï, " Colloque international sur les Hétérocycles oxygénés, Lyon, 1955," Centre National de la Recherche Scientifique, Paris, 1957, p. 111.