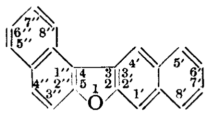
93. *Identification of* " iso*Dinaphthylene Oxide* " *as Dinaphtho*(2′ : 3′-2 : 3)(1″ : 2″-4 : 5)*furan; Some Functional Derivatives of the Latter.*

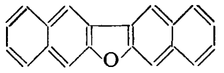
By Ng. Ph. Buu-Hoï.

" *iso*Dinaphthylene oxide " resulting from the calcium oxide-catalysed oxidodehydration of β-naphthol (Clemo and Spence, *J.*, 1928, 2811) is found to be identical with dinaphtho(2′ : 3′-2 : 3)(1″ : 2″-4 : 5)furan, prepared by zinc dust distillation of the corresponding 5 : 8-quinone. Several functional derivatives of the latter have been prepared from 2 : 3-dichloro-1 : 4-naphthaquinone; this quinone proved to be a sensitive reagent for the characterisation of β-naphthols having a free adjacent α-position.

The six isomeric dinaphthofurans have come under consideration in this Institute because of their molecular resemblance to the corresponding dibenzofluorenes, some of which are known inhibitors of the growth of grafted tumours (Badger *et al.*, *Proc. Roy. Soc.*, 1942, *B*, **130**, 255; Haddow, quoted by Cook and Stephenson, *J.*, 1949, 842), and of the carcinogenic action of methylcholanthrene and other similar hydrocarbons (Lacassagne, Buu-Hoï, and Cagniant, *Compt. rend. Soc. Biol.*, 1944, **138**, 16; Lacassagne, Buu-Hoï, and Rudali, *Brit. J. Exp. Path.*, 1945, **26**, 5). The most accessible dinaphthofuran is " *iso*dinaphthylene oxide," prepared by Clemo and Spence (*J.*, 1928, 2811) by prolonged heating above 280° of β-naphthol in the presence of alkali-earth oxides. The fact that this substance underwent chromic oxidation to a *p*-monoquinone, as well as the interpretation of spectroscopic data (Clemo, Cockburn, and Spence, *J.*, 1931, 1265), led those authors to give preference to formula (I) for its constitution, rather than the alternative formula (II) :

(I)

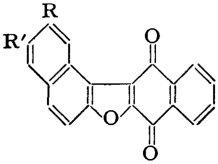




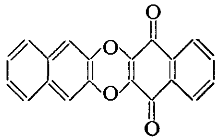
(II)

There has not, however, as yet been any rigid proof for this constitution; confirmation of Clemo and Spence's assumption is now offered by the synthesis of dinaphtho(2′ : 3′-2 : 3)(1″ : 2″-4 : 5)furan (I) and its identification with " *iso*dinaphthylene oxide." Dinaphtho(2′ : 3′-2 : 3)(1″ : 2″-4 : 5)furan-1′ : 4′-quinone (III; R = R′ = H) was prepared by condensation of β-naphthol with 2 : 3-dichloro-1 : 4-naphthaquinone in pyridine solution (Eistert, *Ber.*, 1947, **80**, 52), and found identical with the quinone prepared from " *iso*dinaphthylene oxide " by oxidation. That β-naphthol links with 2 : 3-dichloro-1 : 4-naphthaquinone at the 1- and not the 3-position is proved by the inability of 1-substituted 2-naphthols (for example, 1-methyl-2-naphthol) to give such furan derivatives. Conversely, zinc dust distillation of a sample of the quinone prepared by Eistert's method yielded a compound $C_{20}H_{12}O$ which was found identical with " *iso*dinaphthylene oxide."

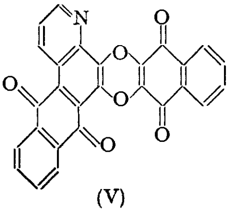
The formation of furan derivatives from 2 : 3-dichloro-1 : 4-naphthaquinone is characteristic of homologues of β-naphthol having a free adjacent α-position, as shown by the ready preparation of 6″-methyl- (III; R = H, R′ = Me), 6″-*n*-propyl- (III; R = H, R′ = Pr^n), and 6″-*tert.*-butyl-dinaphtho(2′ : 3′-2 : 3)(1″ : 2″-4 : 5)furan-1′ : 4′-quinone (III; R = H, R′ = Bu^t) from 6-methyl-, 6-*n*-propyl-, and 6-*tert.*-butyl-2-naphthol respectively. From 6-bromo-2-naphthol, the 6″-bromo-quinone (III; R = H, R′ = Br) could also be prepared without loss of bromine, whereas with 2-hydroxy-3-naphthoic acid the non-substituted quinone (III; R = R′ = H) formed by partial decarboxylation could be isolated. In the case of heteronuclear amino-derivatives of β-naphthol, routine furan cyclisation was accompanied by the reaction of another molecule of 2 : 3-dichloro-1 : 4-naphthaquinone upon the amino-group (cf. Plagemann, *Ber.*, 1882, **15**, 484; Brass, *Ber.*, 1912, **45**, 2531; Fries and Ochwat, *Ber.*, 1923, **56**, 1317; Buu-Hoï, *Bull. Soc. chim.*, 1944, **11**, 578); thus, from 7-amino-2-naphthol, 7″-(2-chloro-1 : 4-naphthaquinon-3-yl)dinaphtho-(2′ : 3′-2 : 3)(1″ : 2″-4 : 5)furan-1′ : 4′-quinone was obtained.



(III)



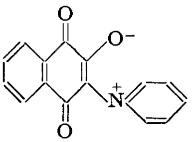
(IV)



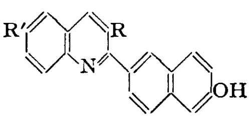
(V)

It was interesting to investigate whether the three dihydroxynaphthalenes bearing both hydroxyl groups in the β-position would give double furan cyclisation with two molecules of 2 : 3-dichloro-1 : 4-naphthaquinone : in none of the three cases was this found possible. 2 : 3-Dihydroxynaphthalene yielded dinaphtho(2′ : 3′-2 : 3)(2″ : 3″-5 : 6)dioxin-1 : 4-quinone (IV), a reaction similiar to that observed by Ullmann and Ettisch (*Ber.*, 1921, **54**, 259) with catechol; 2 : 6- and 2 : 7-dihydroxynaphthalene yielded 6″-hydroxy- (III; R = H, R′ = OH) and 7″-hydroxy-dinaphtho(2′ : 3′-2 : 3)(1″ : 2″-4 : 5)furan-1′ : 4′-quinone (III; R = OH, R′ = H), whether one or two molecules of 2 : 3-dichloro-1 : 4-naphthaquinone were used. The methyl ethers of the last two substances could be prepared either by treatment with methyl sulphate of their deep blue solutions in aqueous sodium hydroxide, or more directly by condensation of 6-methoxy- and 7-methoxy-2-naphthol with 2 : 3-dichloro-1 : 4-naphthaquinone.

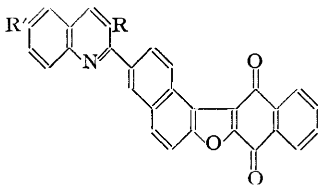
Whereas 2 : 3-dichloro-1 : 4-naphthaquinone is known to react with pyridine to give the betaine (VI) (Ullmann and Ettisch, *loc. cit.*), normal condensations were observed on the one hand with alizarin blue (3 : 4-dihydroxy-4′-aza-1 : 2-benzanthra-9 : 10-quinone) to form the benzodioxin compound (V), and on the other hand, with 6 : 2′-quinolyl-2-naphthol and several of its derivatives (VII) to give the expected furan compounds (VIII). The affinity of the chlorine atoms in 2 : 3-dichloro-1 : 4-naphthaquinone towards heterocyclic nitrogen is thus inferior to that towards phenolic groups.



(VI)



(VII)



(VIII)

A characteristic property of all the furan-quinones mentioned in this work is the deep blue colour of their solutions in pure sulphuric acid. This colour test (which is also given by brasanquinone and its derivatives) might be of interest for the detection of a β-naphthol group having the adjacent α-position free, a problem frequently encountered in the study of certain natural products.

EXPERIMENTAL

Dinaphtho(2′ : 3′-2 : 3)(1″ : 2″-4 : 5)*furan*-1′ : 4′-*quinone*.—(a) *By Eistert's method.* Eistert's procedure (*loc. cit.*) was modified in the following way: A mixture of 2 : 3-dichloro-1 : 4-naphthaquinone (2·3 g.), β-naphthol (1·5 g.), and anhydrous pyridine (10 c.c.) was cautiously heated to the b. p., whereon a violent reaction set in, the colour of the solution changing to deep brown-red. The mixture was refluxed for a further hour; after cooling, the orange crystalline cake was treated with methanol, collected, washed with water, and recrystallised from acetic acid. The shiny orange-yellow needles obtained (2·8 g.) had m. p. 271—272°, and gave an intense greenish-blue colour with sulphuric acid.

(b) *From* " iso*dinaphthylene oxide.*" Oxidation of this compound was much shortened when potassium dichromate and dilute sulphuric acid (Clemo and Spence, *loc. cit.*) were replaced by chromic acid in acetic acid medium. The m. p. of the quinone obtained (271—272°) was not depressed on admixture with the sample mentioned above; the colour with sulphuric acid was also the same.

Dinaphtho(2′ : 3′-2 : 3)(1″ : 2″-4 : 5)*furan* (I).—An intimate mixture of one part of the quinone prepared by Eistert's method with ten parts of dry zinc dust was heated in a vacuum, and the yellow distillate crystallised several times from acetic acid; the pale yellow needles obtained had m. p. 159°, alone or mixed with "*iso*dinaphthylene oxide." The yellow colour of this compound is probably due to traces of an impurity (possibly perylene), as a sample purified by chromatography was almost colourless. The molecular compound with 1 : 3 : 5-trinitrobenzene formed from benzene silky deep orange prisms, m. p. 175°.

6″-*Methyldinaphtho*(2′ : 3′-2 : 3)(1″ : 2″-4 : 5)*furan*-1′ : 4′-*quinone.*—6-Methyl-2-naphthol was prepared from β-methylnaphthalene according to Dziewoński, Schoenówna, and Waldmann (*Ber.*, 1925, **58**, 1213); a solution of this compound (1·8 g.) and 2 : 3-dichloro-1 : 4-naphthaquinone (2·3 g.) in pyridine (10 c.c.) was treated as above; the *quinone* (3 g.) obtained crystallised on cooling, and formed from xylene long silky orange-yellow needles, m. p. 270° (Found : C, 80·6; H, 3·8. $C_{21}H_{12}O_3$ requires C, 80·8; H, 3·8%).

6-n-*Propyl-2-naphthol.*—This *compound* (2 g.) was prepared by demethylation with pyridine hydrochloride (10 g.) of the product from the Clemmensen reduction of 6-propionyl-2-methoxynaphthalene (6 g.); it formed from ligroin silky colourless needles, m. p. 81° (Found: C, 83·6; H, 7·6. $C_{13}H_{14}O$ requires C, 83·9; H, 7·5%). 6″-n-*Propyldinaphtho*(2′ : 3′-2 : 3)(1″ : 2″-4 : 5)*furan*-1′ : 4′-*quinone* was readily soluble in xylene, and formed fine silky orange needles, m. p. 212° (Found : C, 81·0; H, 4·6. $C_{23}H_{16}O_3$ requires C, 81·2; H, 4·7%).

6″-tert.-*Butyldinaphtho*(2′ : 3′ : 2 : 3)(1″ : 2″-4 : 5)*furan*-1′ : 4′-*quinone.*—This *quinone* formed from toluene shiny golden-yellow leaflets, m. p. 239—240° (Found: C, 80·9; H, 5·0. $C_{24}H_{18}O_3$ requires C, 81·3; H, 5·1%); 6-*tert.*-butyl-2-naphthol was prepared according to Buu-Hoï *et al.* (*J. Org. Chem.*, 1950, **15**, 1060).

6″-*Bromodinaphtho*(2′ : 3′-2 : 3)(1″ : 2″-4 : 5)*furan*-1′ : 4′-*quinone* formed from pyridine shiny light orange-yellow, sublimable needles, m. p. 308° (Found : C, 63·3; H, 2·2. $C_{20}H_9O_3Br$ requires C, 63·7; H, 2·4%); a compound with similar properties was obtained by chromic oxidation of " dibromo*iso*dinaphthylene oxide " (Clemo and Spence, *loc. cit.*), but with a somewhat lower m. p. (300—301°).

7″-(2-*Chloro*-1 : 4-*naphthoquinon*-3-*yl*)*dinaphtho*(2′ : 3′-2 : 3)(1″ : 2″-4 : 5)*furan*-1′ : 4′-*quinone.*—A solution of 7-amino-2-naphthol (2 g.) and 2 : 3-dichloro-1 : 4-naphthaquinone (4 g.) in pyridine (15 c.c.) was refluxed for 6 hours. After cooling, the precipitate was collected, washed with ethanol, and recrystallised from pyridine or nitrobenzene, to give the *quinone* as fine brown prisms, m. p. > 340°, giving with sulphuric acid a deep blue-violet colour (Found : C, 71·2; H, 3·4. $C_{30}H_{14}O_5NCl$ requires C, 71·4; H, 2·8%).

7″-*Hydroxydinaphtho*(2′ : 3′-2 : 3)(1″ : 2″-4 : 5)*furan*-1′ : 4′-*quinone.*—A solution of 2 : 7-dihydroxynaphthalene (2 g.) and 2 : 3-dichloro-1 : 4-naphthaquinone (2·3 or 4·6 g.) in pyridine (15 c.c.) was refluxed for 18 hours; the orange precipitate obtained on cooling formed from pyridine silky red, sublimable needles (2 g.), m. p. > 340°, giving with sulphuric acid a Prussian-blue colour (Found : C, 76·0; H, 3·3. $C_{20}H_{10}O_4$ requires C, 76·4; H, 3·2%). The *methyl ether*, prepared by direct methylation or from 7-methoxy-2-naphthol, formed from xylene fine orange needles, m. p. 255—256° (Found : C, 76·5; H, 3·5. $C_{21}H_{12}O_4$ requires C, 76·8; H, 3·7%).

6″-*Hydroxydinaphtho*(2′ : 3′-2 : 3)(1″ : 2″-4 : 5)*furan*-1′ : 4′-*quinone* separated from acetic acid as either red, sharp prisms, or silky orange needles, m. p. 317—318° (decomp.) (Found : C, 76·2; H, 3·2%). The *methyl ether* formed from xylene orange-yellow prisms, m. p. 281—282° (Found : C, 76·5; H, 3·6%).

Dinaphtho(2′ : 3′-2 : 3)(2″ : 3″-5 : 6)*dioxin*-1 : 4-*quinone* formed from pyridine shiny brown-red, sublimable needles, m. p. > 340°, giving with sulphuric acid a violet colour, changing to brown (Found : C, 76·1; H, 3·1. $C_{20}H_{10}O_4$ requires C, 76·4; H, 3·2%). The *diquinone* (V), prepared from alizarin-blue (4 g.) and 2 : 3-dichloro-1 : 4-naphthaquinone (2 g.) in pyridine (15 c.c.), formed dark blue microcrystals, m. p. > 340° (Found : C, 72·4; H, 2·3. $C_{27}H_{11}O_6N$ requires C, 72·8; H, 2·5%).

6''-(2-Quinolyl)dinaphtho(2' : 3'-2 : 3)(1'' : 2''-4 : 5)*furan*-1' : 4'-*quinone* (VIII; R = R' = H).—6-2'-Quinolyl-2-naphthol was prepared by demethylation of the corresponding methyl ether (Buu-Hoï, *Rec. Trav. chim.*, 1949, **68**, 759) with pyridine hydrochloride, and basification with aqueous ammonia of the orange-yellow, water-insoluble hydrochloride. The *quinone* formed with 2 : 3-dichloro-1 : 4-naphthaquinone yielded, from pyridine, silky orange needles, m. p. 302—303° (Found : C, 81·8; H, 3·6. $C_{29}H_{15}O_3N$ requires C, 81·9; H, 3·5%).

6''-(6-Bromo-2-quinolyl)dinaphtho(2' : 3'-2 : 3)(1'' : 2''-4 : 5)*furan*-1' : 4'-*quinone* (VIII; R = H, R' = Br).—6-(6-Bromo-2-quinolyl)-2-naphthol was prepared as above; the *quinone* formed from pyridine shiny orange prisms, m. p. 336° (Found : N, 2·7. $C_{29}H_{14}O_3NBr$ requires N, 2·8%).

6''-(3-Methyl-2-quinolyl)dinaphtho(2' : 3'-2 : 3)(11' : 2''-4 : 5)*furan*-1' : 4'-*quinone* (VIII; R = Me, R' = H), prepared from 6-(3-methyl-2-quinolyl)-2-naphthol, formed from pyridine silky orange needles, m. p. 284—285° (decomp.) (Found : N, 3·1. $C_{30}H_{17}O_3N$ requires N, 3·2%).

6''-(6-Bromo-3-methyl-2-quinolyl)dinaphtho(2' : 3'-2 : 3)(1'' : 2''-4 : 5)*furan*-1' : 4'-*quinone* (VIII; R = Me, R' = Br).—*6-(6-Bromo-3-methyl-2-quinolyl)-2-naphthol* (VII; R = Me, R' = Br) formed from ethanol shiny colourless needles, m. p. 260—261° (Found: C, 65·6; H, 4·0. $C_{20}H_{14}ONBr$ requires C, 65·9; H, 3·8%); the *quinone* crystallised from pyridine in orange prisms, m. p. 279° (decomp.) (Found : C, 69·1; H, 3·0. $C_{30}H_{16}O_3NBr$ requires C, 69·5; H, 3·1%).

6''-(6-Bromo-3-phenyl-6-quinolyl)dinaphtho(2' : 3'-2 : 3)(1'' : 2''-4 : 5)*furan*-1' : 4'-*quinone* (VIII; R = Ph, R' = Br), prepared from 6-(6-bromo-3-phenyl-2-quinolyl)-2-naphthol, formed from pyridine as fine orange prisms, m. p. 275—276° (decomp.) (Found: C, 72·2; H, 3·2. $C_{35}H_{18}O_3NBr$ requires C, 72·4; H, 3·1%).

In carcinogenesis tests, performed in this Institute, "*iso*dinaphthylene oxide" proved to be inactive, in confirmation of earlier findings by Barry *et al.* (*Proc. Roy. Soc.*, 1935, *B*, **117**, 346).

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