361. *Potential Radiosensitizers: Some Quinones and Related Compounds.*

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Since some quinol bis(disodium phosphates) sensitize growing tissue towards the effects of ionizing radiation, three compounds of this type have been prepared bearing a radioactive atom for metabolic studies. The syntheses of some related compounds containing iodine are also included.

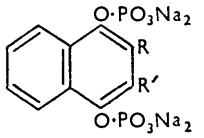
Bromination of the Diels–Alder adduct of toluquinone and butadiene leads to either a tri- or a tetra-bromo-derivative depending on conditions. The structure of each of these compounds has been determined.

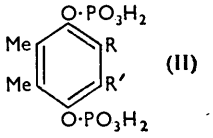
For some years, work in these laboratories has been aimed at the synthesis of compounds which would sensitize growing tissue towards the curative or palliative effects of *X*-irradiation. Injections of cyanide or iodoacetic acid have been reported to sensitize tumour tissues to radiation,[1] and certain iodides,[2] gonadotropic hormone,[3] and fluorescein[4] seemed to have similar properties; investigation of the effect of oxygen tension[5] has led to the practice of oxygen inhalation by patients about to undergo *X*-ray therapy. Cornil

[1] Harker and Moppett, *Austral. J. Exp. Biol.*, 1936, **14**, 15.
[2] Ito, *Japan. J. Obstet. Gyn.*, 1937, **20**, 541.
[3] Narimatsu, *ibid.*, p. 411.
[4] Umanskii, Varshauskii, and Kudokobsev, *Doklady Akad. Nauk S.S.S.R.*, 1949, **65**, 581.
[5] See Hollaender, "Symposium on Radiobiology," Chapman and Hall Ltd., London, 1952, p. 285, for a review.

and Stohl [6] claimed that the radiosensitivity of a cell is related to its nucleic acid content and that the greater the ratio of deoxyribonucleic acid to ribonucleic acid, the higher the sensitivity.

Previous work from these laboratories [7] has shown that 2-methyl-1 : 4-naphthaquinol bis(disodium phosphate) (I; R = Me, R′ = H) inhibited mitosis of chick-heart fibroblast cultures (50% inhibition compared to controls by 4 × 10^{-6}M-solution), and, further, that the antimitotic and chromosome fragmentation effects of 150 r of 220-kv *X*-rays in conjunction with the phosphate (I; R = Me, R′ = H) (2 × 10^{-6}M) were much greater than the sum of the effects due to *twice* the dose of *X*-rays and *twice* the concentration of phosphate acting separately.[8a] The compound (I; R = R′ = H) had the highest order of antimitotic activity yet reported,[9] the concentration causing 50% inhibition being 3 × 10^{-9}M. Both the phosphates (I; R = R′ = H and Me) [10] were potent radiosensitizers.[8b] The halogenated derivatives (I; R = Me or H, R′ = Br) retained the property of mitotic inhibition.[11]

(I) 



(II)

First stages of a clinical trial of the phosphate (I; R = Me, R′ = H) as an adjunct to *X*-ray therapy of inoperable carcinoma of the bronchus have been reported,[12] but the *small* clinical effect observed should not be allowed to diminish the important finding that such an effect as sensitization towards *X*-ray is possible and that, *in vitro*, the effect on growing tissues is reproducible and of an encouragingly high order.

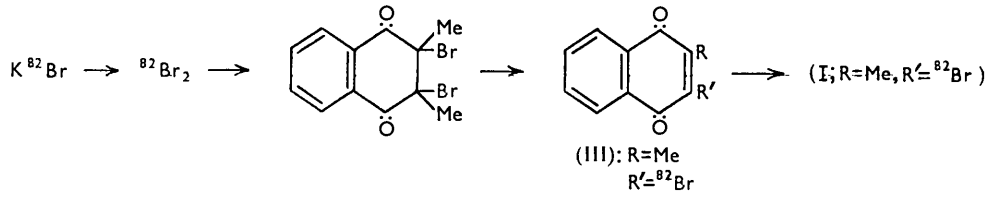
We visualize that an efficient radiosensitizing agent would have to fulfil certain criteria. It must increase those effects of *X*-rays on tissues which are important in the cure or palliation of malignant conditions, especially the effects on mitosis and on chromosome structure; it should be more effective on rapidly growing than on resting tissue; and it should be well tolerated by the patient. The second criterion could be met if the compound were to become concentrated selectively in growing tissue and in an attempt to study this possibility some potential radiosensitizers containing a labelled atom have been prepared.

The metabolism of the phosphate (I; R = Me, R′ = H) containing radio-phosphorus has been studied by Neukomm and his co-workers [13] but the interpretation of the results had to take into account very rapid enzymic dephosphorylation with the liberation of radioactive inorganic phosphate. Moreover, since Jaques, Millar, and Spinks [14] have shown that rats which had been injected with 2-[^{14}C]methyl-1 : 4-naphthaquinone excreted the corresponding quinol bis(disodium phosphate), labelling the compound with ^{32}P had serious drawbacks for metabolic studies. A more reliable indication of the metabolism of the salt (I; R = Me, R′ = H) would follow from a study of the distribution of the compound bearing ^{14}C in the 2-methyl group and starting with the corresponding quinone (made available to us by the generosity of Dr. Wright Langham, of the Los Alamos Scientific Laboratory), 2-[^{14}C]methyl-1 : 4-naphthaquinol bis(disodium phosphate) (I; R = $^{14}CH_3$, R′ = H) was prepared by conventional methods.

In another approach we sought to make use of ^{82}Br (an energetic γ-emitter) instead of the very weak β-emitter ^{14}C. 2-Bromo-3-methyl-1 : 4-naphthaquinol bis(dihydrogen

[6] Cornil and Stohl, *Presse Med.*, 1951, **59**, 933.
[7] Mitchell and Simon-Reuss, *Nature*, 1947, **160**, 98.
[8] *Idem*, *Brit. J. Cancer*, 1952, **6**, (*a*) 305; (*b*) 317.
[9] Friedmann, Marrian, and Simon-Reuss, *Brit. J. Pharmacol.*, 1948, **3**, 263.
[10] Marrian, *J.*, 1954, 760.
[11] Friedmann, Marrian, and Simon-Reuss, *Biochim. Biophys. Acta*, 1952, **8**, 680.
[12] Mitchell, *Brit. J. Cancer*, 1953, **7**, 313.
[13] Neukomm, Peguiron, Lerch, and Richard, *Arch. internat. Pharmacodyn. Therapie*, 1953, **93**, 373; Neukomm, Radiobiology Symposium, Butterworths Scientific Publns., London, 1954, p. 189.
[14] Jaques, Millar, and Spinks, *Schweiz. Med. Woch.*, 1954, **29**, 792.

phosphate) had already been prepared,[11] and this synthesis was modified for the preparation of the corresponding compound containing ^{82}Br as follows:



Studies of the metabolism of the phosphates (I; R = $^{14}CH_3$, R′ = H) and (I; R = Me, R′ = ^{82}Br) have been briefly reported.[15] ^{82}Br, a γ-emitter, has the disadvantage of a short half-life (35 hours) and ^{14}C the disadvantages associated with low-energy β-emission (0·156 mev) and it was felt that the labelling of potentially interesting compounds with ^{131}I (a β- and γ-emitter of half-life 8·0 days) might combine ease of detection and estimation with even a possible therapeutic dose of radiation derived from the compound itself (cf. ^{131}I-iodide which is used in the therapy of carcinoma of the thyroid gland).

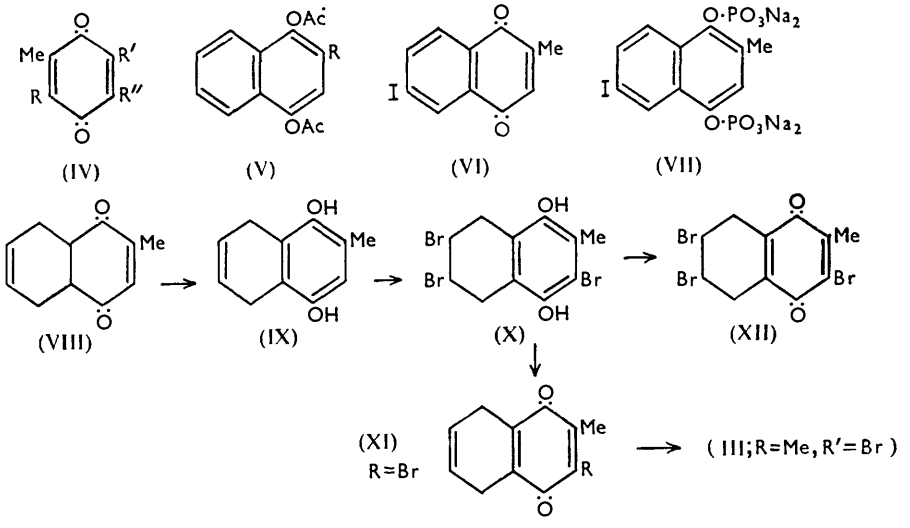
As a model compound the synthesis of 2 : 3-di-iodo-5 : 6-dimethylbenzoquinol bis(dihydrogen phosphate) (II; R = R′ = I) was undertaken. 2 : 3-Dibromo-5 : 6-dimethylbenzoquinone reacted readily with sodium iodide in boiling ethyl methyl ketone, to give the dark red di-iodo-quinone which was reduced to the quinol and phosphorylated. A satisfactory yield of the phosphate (II; R = R′ = I) resulted. When the synthesis was undertaken with sodium ^{131}I-iodide, the need to conserve radioactivity suggested that only the theoretical amount of sodium iodide should be used. This resulted in an even better yield of crystalline di-iodo-quinone but the lower melting point and analytical figures indicated contamination with about 3% of the starting dibromo-quinone. This was felt to be unimportant, especially as reduction and phosphorylation still gave an excellent yield of the phosphate (II; R = R′ = ^{131}I). Contamination was again evident from the analytical figures and this was confirmed by paper chromatography. Autoradiography of the paper strip showed that more than 95% of the radioactivity of the sample was associated with the main component, that traces were present in material behaving like the corresponding quinone, but that none was present as iodide ion.

This synthesis suggested that bromine atoms attached to the quinone ring could be replaced by iodine provided that the oxidation–reduction potential of the quinone–quinol was lower than that of the iodide–iodine system. This condition was not fulfilled by 5-bromo- or 5-chloro-toluquinone (IV; R = R′ = H, R″ = Br or Cl), by tribromotoluquinone (IV; R = R′ = R″ = Br), or by 5-bromo-2 : 3-dimethyl-1 : 4-benzoquinone (IV; R = Me, R′ = H, R″ = Br), all of which liberated iodine when treated with sodium iodide in acetone.

Preliminary metabolic experiments with the phosphates (I; R = Me, R′ = ^{82}Br) and (II; R = R′ = ^{131}I) showed that the halogen attached to the quinol ring was rapidly liberated as halide ion.[15] Simple ion interchange between the bromo-quinone (III; R = Me, R′ = Br) and salts contained in the body was unlikely to account for this since attempts to prepare the iodo-quinone (III; R = Me, R′ = I) by an exchange reaction between 2-bromo-3-methyl-1 : 4-naphthaquinone (III; R = Me, R′ = Br) and iodide ion were not successful. A possible mechanism for liberation of halide ion *in vivo* involves enzymic dephosphorylation to the quinol which would immediately equilibrate with the corresponding quinone. The halogenated quinone (III; R = Me, R′ = Br) or (IV; R = Me, R′ = R″ = I) might then be attacked by thiol-containing material with elimination of halide ion. 2-Chloro- and 2 : 3-dichloro-1 : 4-naphthaquinones (III; R = Cl, R′ = H; and R = R′ = Cl) react with thiols in this way,[16] and so does chloranil,[17] and it was found

[15] Maxwell, "Second Radioisotopes Conference, 1954," Butterworths Scientific Publns., London, 1954, Vol. I, p. 200.
[16] Fieser and Brown, *J. Amer. Chem. Soc.*, 1949, **71**, 3609.
[17] Schubert, *ibid.*, 1947, **69**, 712.

that the quinone (III; R = Me, R′ = Br) reacted smoothly with sodium mercaptoacetate to give the acid (III; R = Me, R′ = S·CH_2·CO_2H) identical with a specimen prepared from 2-methyl-1 : 4-naphthaquinone and mercaptoacetic acid.[18] The quinone (IV; R = Me, R′ = R″ = I) also reacted with sodium mercaptoacetate to give the quinone-acid (IV; R = Me, R′ = R″ = S·CH_2·CO_2H), isolated and purified as the derived quinol. The lability of bromine in compounds analagous to (I; R = Me, R′ = Br) was also observed by Carrava [19] who showed that 2-bromo-3-methyl-1 : 4-naphthaquinol suffered quantitative loss of bromide under alkaline conditions.



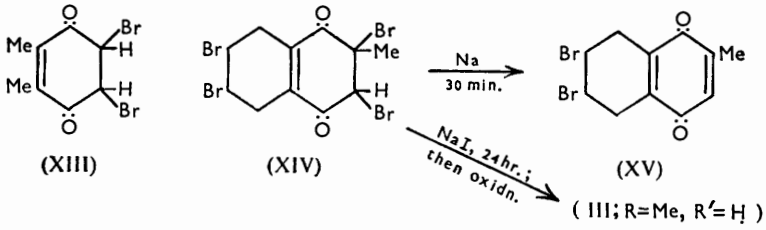
This ready loss of halogen from the phosphates (I; R = Me, R′ = Br) and (II; R = R′ = I) made compounds such as (III; R = CH_2Br, R′ = H) and (V; R = CH_2Br or CH_2I) of little interest as intermediates, but 2-bromomethyl-1 : 4-naphthaquinone (III; R = CH_2Br, R′ = H) was readily obtained by Ziegler bromination of 2-methyl-1 : 4-naphthaquinone in hot acetic anhydride in the presence of dibenzoyl peroxide, and the quinol diacetate (V; R = CH_2Br) from 1 : 4-diacetoxy-2-methylnaphthalene and *N*-bromosuccinimide in carbon tetrachloride. Both compounds decomposed on storage, but the quinol diacetate reacted smoothly with sodium iodide to give 1 : 4-diacetoxy-2-iodomethylnaphthalene (V; R = CH_2I) which was also unstable. No attempts were therefore made to convert these compounds into the corresponding bis(dihydrogen phosphates).

Halogenation of the quinol ring having proved unsatisfactory, attention was turned to the introduction of halogen into the benzenoid ring. Thus 6-methyl-2-naphthylamine was converted in turn into the 2-iodo-compound, the iodo-quinone (VI), and the bis(disodium phosphate) (VII). However, the early introduction of the iodine atom into the molecule and the low overall yield of (VII) rendered this synthesis of little value for the preparation of a therapeutic agent containing ^{131}I. Attempts to prepare the compound (VI) or (VII) labelled with ^{131}I by exchange reactions between the inactive compounds and ^{131}I-iodine were unsuccessful. Similar failures to prepare iodine-labelled derivatives of 2-methyl-1 : 4-naphthaquinone or the corresponding quinol bis(disodium phosphate) were encountered.

It seemed possible that Diels–Alder adducts between toluquinone and butadiene might be convenient starting materials for the preparation of similar compounds and, although iodo-compounds were not obtained, some interesting observations have been recorded. The adduct (VIII) [20] was isomerised to the quinol (IX) by a trace of hydrobromic acid in hot acetic acid. When this was treated in ether suspension with 3 mols. of bromine in

[18] Fieser and Turner, *J. Amer. Chem. Soc.*, 1947, **69**, 2335.
[19] Carrava, *Gazzetta*, 1943, **73**, 225, 237, 238.

acetic acid, a tribromide (X) crystallised on cooling, the structure of which has been deduced as follows. Its analyses indicated a formula $C_{11}H_{11}O_2Br_3$, and it was soluble in alkali and absorbed ultraviolet light maximally at 290 mμ (ε 4200). This wavelength is close to the maximum absorption of quinol (ε 2970 at 294 mμ) and the naphthaquinol (IX) (ε 3600 at 290 mμ). Treatment of the tribromide (X) with sodium iodide in acetone, followed by gentle oxidation, gave the unstable quinone (XI; R = Br) (cf. Finkelstein [21]). Vigorous oxidation of this by chromic acid in acetic acid [22] gave 2-bromo-3-methyl-1 : 4-naphthaquinone (III; R = Me, R′ = Br) which was identified by comparison with an authentic specimen.[23] The freshly prepared quinone (XI; R = Br) had a typical bromobenzoquinone spectrum ($\varepsilon_{max.}$ = 10,500 at 267 mμ) and the rapid darkening of its colour was



associated with a change in the spectrum to one showing maxima at 245 and 280 mμ (ε 7300 and 7900 respectively) qualitatively very similar to that of 2-bromo-3-methyl-1 : 4-naphthaquinone ($\varepsilon_{max.}$ = 13,700 and 13,200 at 245 and 280 mμ respectively). Further, oxidation of the quinol (X) with dichromate in dilute sulphuric acid at room temperature or bromine in hot acetic acid (cf. Zincke) [24] gave the quinone (XII), whose spectrum showed maximum absorption at 275 mμ (ε 12,900); this absorption is in accord with that of the quinone (XV; $\varepsilon_{max.}$ = 24,000 at 255 mμ) since Braude [25] has shown that introduction of bromine into a quinone ring tends to decrease the extinction coefficient by about 50% and to increase the wavelength of maximal absorption by 10—20 mμ. The residual bromine atom in the quinone (XI; R = Br) appeared unreactive towards iodide ion, a behaviour also shown by the analogue (III; R = Me, R′ = Br).

More vigorous bromination of the quinol (IX) in hot acetic acid gave a colourless compound $C_{11}H_{10}O_2Br_4$, insoluble in alkali and unaffected by mild oxidation. This is considered to be (XIV) on the grounds of its analytical composition, its lack of colour, and its maximal absorption of ultraviolet light at 275 mμ (ε 5300) which accords well with the properties of a similar type of compound, 2 : 3-dibromo-2 : 3-dihydro-5 : 6-dimethyl-1 : 4-benzoquinone (XIII) ($\varepsilon_{max.}$ = 8300 at 275 mμ) obtained by addition of 1 mol. of bromine to 2 : 3-dimethyl-1 : 4-benzoquinone. Moreover, treatment of the compound (XIV) with sodium iodide again eliminated two bromine atoms to give the quinone (XV) (cf. Zincke [26] who prepared 2 : 3-dichloro-1 : 4-naphthaquinone by action of potassium iodide on the corresponding dihydronaphthaquinone tetrachloride). The quinone (XV), when first prepared, had a typical quinone spectrum ($\varepsilon_{max.}$ 25,000 at 255—256 mμ) but on storage the compound changed to a mixture of indefinite melting point and became only partially soluble in alcohol. These changes were not associated with the pronounced darkening shown by the compound (XI; R = Br) but recall the dimerisation of 2-methyl-1 : 4-naphthaquinone in sunlight. More prolonged treatment of the tetrabromo-compound (XIV) with sodium iodide eliminated all four bromine atoms. The resulting compound, which rapidly changed colour from yellow to purple in air and was doubtless 5 : 8-dihydro-2-methyl-1 : 4-naphthaquinone (XI; R = H) gave 2-methyl-1 : 4-naphthaquinone (III;

[20] Fieser and Chang, *J. Amer. Chem. Soc.*, 1942, **64**, 2043.
[21] Finkelstein, *Ber.*, 1910, **43**, 1530.
[22] Fieser, Campbell, and Fry, *J. Amer. Chem. Soc.*, 1939, **61**, 2206.
[23] Adams, Giessmann, Baker, and Teeter, *ibid.*, 1941, **63**, 533.
[24] Zincke, *Ber.*, 1887, **20**, 1777.
[25] Braude, *J.*, 1945, 490.
[26] Zincke, *Annalen*, 1889, **255**, 356, 369.

R = Me, R′ = H) on oxidation with chromic acid. These reactions and properties complete the identification of 2 : 3 : 6 : 7-tetrabromo-2 : 3 : 5 : 6 : 7 : 8-hexahydro-2-methyl-1 : 4-naphthaquinone (XIV).

Under the usual conditions, the quinol (IX) readily formed a bis(dihydrogen phosphate), isolated as its tetra*cyclo*hexylamine salt. Treatment of an aqueous solution of the latter with excess of sulphuric acid caused the mono*cyclo*hexylamine salt to crystallise—a derivative apparently less sensitive to light than the original salt.

Experimental

2-[^{14}C]*Methyl*-1 : 4-*naphthaquinol Bis*(*barium Phosphate*).—2-[^{14}C]Methyl-1 : 4-naphthaquinone (57·8 mg. containing 1 mc of ^{14}C) was added to a solution of 2-methyl-1 : 4-naphthaquinone (940 mg.) in pure dry ether (60 c.c.). The quinone was reduced by shaking it with platinum oxide and hydrogen at atmospheric pressure. Uptake ceased when 131 c.c. had been absorbed (req., 131 c.c. at N.T.P.). The colourless ethereal solution was decanted into a flask filled with nitrogen, and the solvent removed *in vacuo* over nitrogen. Dimethylaniline (12 c.c.) was added and the mixture magnetically stirred in an ice-bath with exclusion of moisture during the addition (30 min.) of freshly distilled phosphorus oxychloride (10 c.c.), then stirred at room temperature over-night. Ice was added, followed by 5N-sodium hydroxide to pH 8—9. Stirring was continued for 3 hr., with occasional addition of alkali to maintain the slightly alkaline conditions, the organic layer was separated and washed with N-sodium hydroxide (2 × 10 c.c.), and the combined aqueous phases were washed with methylene chloride (2 × 20 c.c.). The aqueous phase was brought to neutrality by addition of concentrated hydrochloric acid. Ammonium chloride (6 g.) and calcium chloride (6 g. of the hexahydrate) were then added, the precipitate was filtered off and washed with water (5 × 10 c.c.). The combined filtrates were acidified with concentrated hydrochloric acid (12 c.c.) with stirring and extracted with butan-1-ol (4 × 20 c.c.). The extracts were then extracted with N-sodium hydroxide (4 × 20 c.c.), the aqueous phases neutralised with concentrated hydrochloric acid, and the volume reduced to about 40 c.c. by evaporation *in vacuo* over nitrogen. Ammonium chloride (2·0 g.) and barium chloride (3·5 g. of dihydrate) were then added, and the solution was clarified by filtration through Hyflo and boiled. The *barium salt* crystallized (reverse solubility); the yield was 1·5 g. (38%) after a further recrystallization from water (Found, in material dried *in vacuo* at room temperature: C, 19·7; H, 2·9; P, 9·05. $C_{11}H_8O_8P_2Ba_2,4\frac{1}{2}H_2O$ requires C, 19·3; H, 2·5; P, 9·0%). Ultraviolet max. at 226 (ε 45,500) and 290 mμ (ε 5600) in 0·01N-HCl.

A solution of the sodium salt was obtained by ion-exchange over Dowex 50 (Na form). The radioactive and chemical purity of such a solution was tested by paper chromatography (descending) on Whatman No. 1 in saturated ammonium sulphate (80 vol.), M-sodium acetate (20 vol.) and *iso*propyl alcohol (2 vol.). Located by the photographic technique described by Markham and Smith [27] (except that an unfiltered mercury discharge tube was used as the light source), the main spot had R_F 0·55 and was contaminated by traces of material remaining near the origin. More than 99% of the radioactivity of the solution was associated with the main spot, the rest being associated with the slow-moving material. The specific activity of the material was shown to be 0·44 μc/mg. of the tetrasodium salt compared to the calculated value of 0·41 μc/mg.

2-[^{82}Br]*Bromo*-3-*methyl*-1 : 4-*naphthaquinone*.—All reactions involving ^{82}Br were carried out in a well-ventilated hood behind 2 inches of lead. The initial oxidation of potassium bromide to bromine is an adaptation of the method described by Twombly and Schoenewaldt.[28]

Potassium [^{82}Br]bromide (1·4 g. containing 250 mc of ^{82}Br) was dissolved in water (10 c.c.) in a 100 c.c. flask fitted with dropping funnel and gas-inlet and -exit tubes. The gas inlet was branched to the top of the dropping funnel to avoid pressure differences. The contents of the flask were warmed to 40° and stirred during the slow addition of a solution of manganese dioxide (2·0 g.) in concentrated sulphuric acid (20 c.c.) from the funnel. The liberated bromine was transferred by a slow stream of nitrogen through a sulphuric acid drying-tube into a 100 c.c. flask containing 2-methyl-1 : 4-naphthaquinone (1·0 g.), anhydrous sodium acetate (2·0 g.), and acetic acid (15 c.c.), the whole being immersed in liquid air. The exit tube from this flask led through a safety tube to two gas traps containing acetic acid. After final addition of the

[27] Markham and Smith, *Biochem. J.*, 1949, **45**, 294.
[28] Twombly and Schoenewaldt, *Cancer*, 1950, **3**, 601.

oxidizing mixture, liberation of bromine was completed by warming to 70°. When all the bromine had been transferred, the reaction flask was removed from the liquid-air bath, disconnected from the rest of the apparatus, and fitted with an efficient reflux condenser and soda-lime tube. As the bromine melted, acetic acid (5 c.c.) was added and the whole warmed to 50° in a water-bath. After 3 hr., the contents of the flask were cooled and water added to precipitate the quinone, which was filtered off in a tall, cylindrical, sintered-glass funnel. The above technique is adapted from the published method.[23]

2-[^{82}Br]*Bromo*-3-*methyl*-1 : 4-*naphthaquinol Bis*(*disodium Phosphate*).—A rubber teat was placed over the stem of the filter funnel containing the quinone described above, and dry ether (70—80 c.c.) added. Anhydrous calcium sulphate was added (20 g.), the ethereal solution dried by gentle stirring, the rubber teat removed, and the solution allowed to filter into a dry flask (100 c.c. capacity). Reduction to the quinol and subsequent phosphorylation were carried out as described for the ^{14}C-compound above, except that the phosphorus oxychloride was diluted with an equal volume of dry toluene before addition. Before hydrolysis next day, solvents were removed by distillation *in vacuo* over nitrogen, and the residue was treated with ice and alkali as described. Extractions into and out of butanol were carried out by mechanical stirring in the separating funnel to avoid handling. The final alkaline extracts, evaporated to half bulk, were treated with alcohol to turbidity, and the whole was chilled overnight. Colourless hydrated needles of the *bis*(*disodium phosphate*) resulted (yield 34%) (Found, in material dried *in vacuo* at room temperature: C, 21·0; H, 3·2; P, 9·4. $C_{11}H_7O_8P_2BrNa_4,7H_2O$ requires C, 21·0; H, 3·4; P, 9·9%). Ultraviolet max. at 232 (ε 70,000) and 290 mμ (ε 5800) in 0·01N-HCl. These figures agree with those obtained from a specimen of the free acid corresponding to the above salt which had been prepared previously.[11] The material moved as a single spot in the solvent system described above (R_F 0·39) and more than 95% of the radioactivity of the sample was shown to be associated with this spot (measured by autoradiography of the paper strip on Ilford *X*-ray film).

2 : 3-*Di*-*iodo*-5 : 6-*dimethyl*-1 : 4-*benzoquinone*.—2 : 3-Dibromo-5 : 6-dimethyl-1 : 4-benzoquinone (5·0 g.) and sodium iodide (7 g.) were gently refluxed overnight in ethyl methyl ketone (125 c.c.; redistilled). The solvent was evaporated *in vacuo*, and the residue suspended in acetone and poured into water. The red-brown crystals were filtered off, washed with water, and recrystallized from hot alcohol (yield, 3·0 g., 45·5%; m. p. 157—158°).

For analysis, the *compound* was recrystallized twice more from alcohol and formed dark red needles, m. p. 159·5—160° (Found, after drying *in vacuo* at room temperature for 2 hr.: C, 25·0; H, 1·6; I, 66·4. $C_8H_6O_2I_2$ requires C, 24·8; H, 1·6; I, 65·4%). The same reaction, carried out with the dibromoquinone (1·0 g.) and sodium iodide (1·0 g.), gave (after recrystallization from alcohol) 0·83 g. (62%) of red prisms, m. p. 148—149°. This material contained 3·0% of bromine, presumably as unchanged dibromoquinone. This was the scale on which the reaction with sodium [^{131}I]iodide was carried out.

2 : 3-*Di*-*iodo*-5 : 6-*dimethyl*-1 : 4-*benzoquinol Bis*(*dihydrogen Phosphate*).—The above di-iodoquinone (3·5 g.) was reduced in ether by shaking it with aqueous sodium dithionite and the washed and dried quinol phosphorylated as described above for the [^{82}Br]bromo-compound. The mixture was evaporated *in vacuo* at 100° and the resulting gum dissolved in methylene chloride, treated with ice, and brought to pH 8—9 by adding aqueous sodium hydroxide to the stirred mixture. During 3 hr., further additions of alkali kept the solution just alkaline to phenolphthalein. A solution of barium chloride (20 g.) in water was next added, the precipitate separated at the centrifuge, and an equal volume of alcohol added to the supernatant liquid. The precipitated bis(barium phosphate) was collected (centrifuge), washed, and dried (4·9 g., 66%). This salt (3·9 g.) was converted into the acid by percolation through a column of Dowex 50 (H^+ form), and the eluate evaporated to small bulk *in vacuo* over nitrogen. The *compound* separated in colourless prisms, m. p. 242° (decomp.) (600 mg., 52%). After one recrystallization from hot water, it had m. p. 242·5° (decomp.) (Found, in material dried *in vacuo* at room temperature for 2 hr.: C, 17·9; H, 1·8; I, 46·2. $C_8H_{10}O_8P_2I_2$ requires C, 17·5; H, 1·8; I, 46·2%). Repetition of this preparation with the slightly impure radioactive di-iodoquinone gave the labelled compound in similar yield.

5-*Bromotoluquinone*.—Toluquinone (1·0 g.; steam-distilled) was treated in acetic acid (5 c.c.) with bromine (0·45 c.c.) in acetic acid (5 c.c.). Anhydrous sodium acetate (1·0 g.) was added immediately, and the whole warmed till reaction began and left on the steam-bath for 5 min. The solution was poured into water and stirred till the precipitate solidified, and the solid recrystallized from alcohol. The *compound* formed yellow prisms (350 mg., 23%), m. p. 99—100° after softening. For analysis, one recrystallization from hexane raised the m. p. to

105—107° (Found, in material dried *in vacuo* at room temperature, under which conditions the compound is volatile: C, 42·0; H, 2·5; Br, 39·6. $C_7H_5O_2Br$ requires C, 41·8; H, 2·5; Br, 39·75%). The compound is also easily prepared as follows. Toluquinone (1·0 g.) in acetic acid (5 c.c.) was treated with hydrobromic acid in acetic acid (2 c.c.; 50% w/v) with shaking. The colour was quickly discharged, at which point a solution of potassium dichromate (5 g.) and sulphuric acid (2 c.c.) in water (50 c.c.) was added. The resulting solution was chilled in ice, and the crystalline solid filtered off, and washed well with water and then with alcohol (yield, 1·1 g., 67%; m. p. 103—105°).

5-Chlorotoluquinone.—The method reported by Cason, Allen, and Goodwin [29] appeared unnecessarily cumbersome so the compound was prepared as follows: toluquinone (5·0 g.) in acetic acid (25 c.c.) was stirred and treated dropwise with concentrated hydrochloric acid (15 c.c.). 5-Chlorotoluquinol crystallized and was dissolved by warming. Potassium dichromate (25 g.) and sulphuric acid (10 c.c.) in water (250 c.c.) were next added and the whole allowed to cool. 5-Chlorotoluquinone crystallized in 66% yield (m. p. 105—106·5°; Cason *et al.*[29] give 103—104°).

3 : 5 : 6-Tribromotoluquinone.—The conditions described above for the first preparation of 5-bromotoluquinone were repeated, but with twice as much bromine and sodium acetate. Worked up as before, the compound formed yellow prisms (30%), m. p. 233° (decomp.) after two recrystallizations from alcohol followed by sublimation at 140—160°/1 mm. (Found, in material dried *in vacuo* at 50°: C, 23·9; H, 0·9; Br, 66·8. Calc. for $C_7H_3O_2Br_3$: C, 23·4; H, 0·8; Br, 66·8%). Fichter and Rinderspacher [30] give m. p. 234°.

2 : 3-Dibromo-2 : 3-dihydro-5 : 6-dimethyl-1 : 4-benzoquinone.—2 : 3-Dimethyl-1 : 4-benzoquinone (1·0 g.) in acetic acid (5 c.c.) was warmed with bromine (1·2 g.) in acetic acid (5 c.c.). When the colour had been discharged, the solution was poured into water, and the pale yellow prisms were filtered off, washed with water, and dried in air (yield 1·75 g., 80%; m. p. 100—102°). After two sublimations *in vacuo* and one recrystallization from hexane, the *compound* had m. p. 104—105° (Found, in material dried *in vacuo* at room temperature: C, 32·6; H, 2·9; Br, 53·7. $C_8H_8O_2Br_2$ requires C, 32·4; H, 2·7; Br, 54·0%). Ultraviolet max. at 275 mμ (ε 8300).

5-Bromo-2 : 3-dimethyl-1 : 4-benzoquinone.—The above dibromo-compound (1·7 g.) was shaken overnight with a solution of anhydrous sodium acetate (1·0 g.) in acetic acid (10 c.c.). The whole was poured into water and scratched. The *product* formed orange prisms (600 mg., 49%), m. p. 42—43° not raised by recrystallization from alcohol (Found, in material dried *in vacuo* at room temperature: C, 45·0; H, 3·9; Br, 37·55. $C_8H_7O_2Br$ requires C, 44·5; H, 3·7; Br, 37·0%).

2-Carboxymethylthio-3-methyl-1 : 4-naphthaquinone.—Conditions described by Fieser and Turner [18] were followed except that 2-bromo-3-methyl-1 : 4-naphthaquinone was used as starting material. The compound was isolated in 49% yield with m. p. 156—159° raised to 159—161° by recrystallization from benzene. The m. p. was not depressed on admixture with an authentic specimen.

2 : 3-Dicarboxymethylthio-5 : 6-dimethyl-1 : 4-benzoquinol.—Mercaptoacetic acid (0·62 c.c.; redistilled) was neutralized with sodium hydroxide and slowly added to a solution of 2 : 3-diiodo-5 : 6-dimethyl-1 : 4-benzoquinone (1·24 g.) in alcohol (10 c.c.). The mixture was refluxed for 1½ hr., the solvent distilled off *in vacuo*, and the dark residue taken up in a mixture of aqueous sodium dithionite and ether. The ether layer was removed, the aqueous phase was extracted 4 times with ether, and the extracts were combined with the original ether phase. The combined extracts were shaken with M-sodium carbonate (4 × 10 c.c.), and the alkaline extracts brought to pH 3—4 by addition of acetic acid and concentrated hydrochloric acid. This solution was extracted 4 times with ether, and the extracts were dried, boiled with charcoal, and filtered. Evaporation left a red solid which was recrystallized from 50% alcohol containing a little dithionite. High-melting, colourless prisms of *2 : 3-dicarboxymethylthio-5 : 6-dimethyl-1 : 4-benzoquinol* were deposited on cooling (0·6 g., 59%), which were recrystallized once more before analysis (Found: C, 45·8; H, 4·4; S, 20·0. $C_{12}H_{14}O_6S_2$ requires C, 45·3; H, 4·4; S, 20·1%).

2-Bromomethyl-1 : 4-naphthaquinone.—2-Methyl-1 : 4-naphthaquinone (1·0 g.), *N*-bromosuccinimide (1·0 g.), and dibenzoyl peroxide (15 mg.) were suspended in acetic anhydride (7·5 c.c.) and heated and shaken at 135° for a few minutes. When the colour lightened, the solution was poured on ice, and the liquid decanted. The yellow solid was triturated with alcohol and recrystallized from alcohol (5 c.c.) (yield, 360 mg., 27·5%). After recrystallization from methyl

[29] Cason, Allen, and Goodwin, *J. Org. Chem.*, 1948, **13**, 403.
[30] Fichter and Rinderspacher, *Helv. Chim. Acta*, 1927, **10**, 40.

alcohol, the *compound* formed yellow needles, m. p. 96° (decomp.) (Found, in material dried *in vacuo* at room temperature: C, 52·3; H, 2·8; Br, 30·3. $C_{11}H_7O_2Br$ requires C, 52·6; H, 2·8; Br, 31·8%). It decomposes when kept.

1 : 4-*Diacetoxy*-2-*bromomethylnaphthalene*.—1 : 4-Diacetoxy-2-methylnaphthalene[31] (8·0 g.), *N*-bromosuccinimide (5·6 g.), and dibenzoyl peroxide (*ca.* 100 mg.) were refluxed in carbon tetrachloride (15 c.c.) for 30 min. under a 200 w lamp. After this time, no active bromine remained in solution. More carbon tetrachloride (15 c.c.) was added, and the whole refluxed and filtered. The yellow prisms deposited on cooling were filtered off, washed, ground with water, filtered off, and dried in air (yield, 6·3 g., 61%; m. p. 138—141·5°). After two recrystallizations from methyl alcohol, the *compound* formed colourless prisms, m. p. 145—146° (Found, in material dried *in vacuo* at 50°: C, 53·5; H, 4·2; Br, 23·8. $C_{15}H_{13}O_4Br$ requires C, 53·4; H, 3·9; Br, 23·7%).

1 : 4-*Diacetoxy*-2-*iodomethylnaphthalene*.—1 : 4-Diacetoxy-2-bromomethylnaphthalene (6·0 g.) was refluxed for 1 hr. with sodium iodide in acetone (60 c.c. of 15% w/v). About half of the acetone was distilled off and the residue poured into water (200 c.c.). The precipitate was filtered off, washed with water, and dried *in vacuo* (yield, 6·7 g., 97%). After recrystallization from alcohol, there were obtained 4·45 g. (64%) of 1 : 4-*diacetoxy*-2-*iodomethylnaphthalene* as pale yellow prisms, m. p. 122—123° (decomp.). For analysis, the compound was recrystallized twice more from alcohol after which it formed almost colourless matted needles, m. p. 125·5° (decomp.) (Found, in material dried *in vacuo* at room temperature: C, 47·1; H, 3·5; I, 33·4. $C_{15}H_{13}O_4I$ requires C, 46·9; H, 3·4; I, 33·0%). The compound decomposes when kept.

2-*Iodo*-6-*methylnaphthalene*.—6-Methyl-2-naphthylamine (7·85 g.) was stirred in dilute sulphuric acid (5·6 c.c. of acid in 78 c.c. of water) at 5°. Sodium nitrite (5 g.) in water was added during *ca.* 30 min. Then urea was added, followed by a concentrated solution of potassium iodide (11·2 g.) in water. The mixture was left at room temperature for 1 hr., heated at 90° for 1 hr., and then left at room temperature overnight. The precipitate was removed, was washed with water, and dissolved in ether, and the solution was treated twice with charcoal. The filtered ethereal solution was evaporated and the residue recrystallized from light petroleum (b. p. 100—120°) (yield, 5·5 g., 42%). Recrystallization gave the *compound* as colourless prisms, m. p. 146—147° (Found: C, 48·9; H, 3·3; I, 47·9. $C_{11}H_9I$ requires C, 49·3; H, 3·4; I, 47·3%).

6-*Iodo*-2-*methyl*-1 : 4-*naphthaquinone*.—2-Iodo-6-methylnaphthalene (2·68 g.) was powdered and treated in acetic acid (15 c.c.) with chromium trioxide (5 g.) in water (3·5 c.c.) and acetic acid (3·5 c.c.), dropwise at $<40°$. The mixture was left at room temperature for 1 hr. and then warmed on a water-bath for 30 min. On cooling, most of the *quinone* crystallized, the remainder being obtained by dilution with water. It was washed with water. Recrystallization from methanol gave 1·1 g. (37%) of yellow needles, m. p. 136—137° (Found: C, 43·7; H, 2·4; I, 43·05. $C_{11}H_7O_2I$ requires C, 44·32; H, 2·37; I, 42·6%).

The identity was proved by oxidation with potassium permanganate which gave 4-iodophthalic acid, m. p. 182° (Found: C, 32·2; H, 2·1; I, 42·6. Calc. for $C_8H_5O_4I,\frac{1}{2}H_2O$: C, 31·9; H, 2·0; I, 42·2%).

6-*Iodo*-2-*methyl*-1 : 4-*naphthaquinol*.—6-Iodo-2-methyl-1 : 4-naphthaquinone (2·6 g.) was shaken in ether with aqueous sodium dithionite until colourless. The ethereal solution was dried (Na_2SO_4) and evaporated. The residue was twice dissolved in dry toluene and evaporated *in vacuo*, and then immediately used as follows:

6-*Iodo*-2-*methyl*-1 : 4-*naphthaquinol Bis*(*disodium Phosphate*).—Dry toluene (10 c.c.) and dimethylaniline (8 c.c.) were added to the above quinol, and the mixture cooled in ice and stirred under nitrogen. Phosphorylation and subsequent isolation of the barium salt closely followed the methods given for the radioactive phosphates described above. All the dibarium salt (2·16 g.) was suspended in water (10 c.c.) and stirred and cooled in ice. Barium ions were removed by sodium sulphate, and the filtrate evaporated *in vacuo* below 40° to small volume. Addition of alcohol gave a white precipitate which was filtered off and dried (1·1 g.). The *compound* recrystallized from methanol–ethanol as colourless needles (0·8 g.) which, although hygroscopic, resolidified in air (Found, in material dried *in vacuo* at 110°: C, 24·5; H, 1·6; P, 11·0; I, 22·2. $C_{11}H_7O_8P_2INa_4$ requires C, 24·1; H, 1·3; P, 11·3; I, 23·2%). Ultraviolet max. at 229 (ε 34,580), 247 (ε 38,050), and 288—292 mμ (ε 5740).

The compound gave one ultraviolet-absorbing spot, with a small cap, on a paper chromatogram [ascending in butan-1-ol (50 vol.), acetic acid (15 vol.), and water (35 vol.) for 17 hr.] (R_F 0·45—0·5)

[31] Anderson and Newman, *J. Biol. Chem.*, 1933, **103**, 405.

Attempted Exchange Reactions with 6-Iodo-2-methyl-1 : 4-naphthaquinone and the Corresponding Quinol Bis(disodium Phosphate).—(*a*) The quinone (4 mg.) in butan-1-ol (1·0 c.c.) was treated with a solution of carrier-free [^{131}I]iodine in butan-1-ol (0·5 c.c.). A similar experiment with carbon tetrachloride as solvent was also set up, together with control tubes containing no quinone in each case. All tubes were shaken overnight under a tungsten lamp and then the solutions were extracted with aqueous sodium thiosulphate (4 times). There was no difference in the radioactivity associated with either phase between the controls and the experimental tubes.

Experiments in which a molar amount of carrier iodine was added gave similar negative results.

(*b*) The phosphate (8 mg.) in water (1 c.c.) was treated with carrier-free [^{131}I]iodine in carbon tetrachloride in the presence of buffers at pH 4, 6, and 9. The tubes were shaken overnight under a tungsten lamp and later examination revealed that no radioactivity was asociated with the aqueous phases. Similar results were obtained with butan-1-ol as the solvent or with the addition of carrier iodine.

Similar experiments with 2-methyl-1 : 4-naphthaquinone or the corresponding quinol bis-(disodium phosphate) were carried out in an attempt to introduce iodine directly into the molecule. All failed.

5 : 8-*Dihydro-2-methyl-1 : 4-naphthaquinol.*—The following modification of the published procedure [20] proved effective. The Diels–Alder adduct of toluquinone and butadiene (16 g.) was dissolved in acetic acid (25 c.c.) and brought to incipient boiling. Hydrobromic acid in acetic acid (10 drops; 50% w/v) was added and a vigorous reaction took place. The quinol crystallized immediately and, when cool, was filtered off, washed with alcohol, and dried at 70° (yield 13·7 g., 86%); it had m. p. 172—173° and ultraviolet max. at 290 mμ (ε 3300) in 95% alcohol.

5 : 8-*Dihydro-2-methyl-1 : 4-naphthaquinol Bis(dihydrogen Phosphate).*—The above quinol (6·0 g.) was phosphorylated by the method detailed above, the dibarium salt being isolated by addition of an equal volume of alcohol to its aqueous solution. After centrifuging, washing, and drying, the salt weighed 19·7 g. (96%). The dibarium salt in water was treated with dilute sulphuric acid until free from barium ions, the mixture filtered, and the filtrate evaporated to dryness *in vacuo* under nitrogen at about 50°. The residue was taken up in a little methyl alcohol, and *cyclo*hexylamine (3 c.c.) added. The *tetra*cyclo*hexylamine salt* of the bis(dihydrogen phosphate) crystallized in colourless prisms, which were washed with a little methyl alcohol. The yield (from 3 g. of the barium salt) was 1·8 g.(48%) and the m. p. *ca.* 212° (decomp.) dependent on the rate of heating. For analysis, the compound was dissolved in a little warm methyl alcohol, and excess of *cyclo*hexylamine added, the common ion effect assisting crystallization; m. p. was then 213° (decomp.) (Found, in material dried *in vacuo* at room temperature: C, 55·1; H, 9·05; N, 7·4; P, 7·95. $C_{11}H_{14}O_8P_2,4C_6H_{13}N,1\frac{1}{2}H_2O$ requires C, 55·3; H, 9·1; N, 7·4; P, 8·15%). Ultraviolet max. at 280 mμ (ε 1000) in 95% alcohol, at 272 mμ (ε 770) in 0·1N-HCl.

The *mono*cyclo*hexylamine salt* was prepared as follows: the tetra*cyclo*hexylamine salt (1·0 g.) was dissolved in water (3 c.c.), and 7N-sulphuric acid (3 c.c.) added. The product crystallized and was washed with a little water and then with alcohol (yield, 400 mg., 69%), forming prisms, m. p. 211—212° (Found, in material dried *in vacuo* at room temperature: C, 45·9; H, 6·5; N, 3·4; P, 13·4%; equiv., 153. $C_{11}H_{14}O_8P_2,C_6H_{13}N,\frac{1}{2}H_2O$ requires C, 46·0; H, 6·3; N, 3·2; P, 13·9%; equiv., 153).

3 : 6 : 7-*Tribromo-5 : 6 : 7 : 8-tetrahydro-2-methyl-1 : 4-naphthaquinol.*—5 : 8-Dihydro-2-methyl-1 : 4-naphthaquinol (1·0 g.) was suspended in ether (8 c.c.) and shaken with bromine (0·91 g.) in acetic acid (3 c.c.) until dissolved. An equal amount of bromine in acetic acid was then added, whereupon crystallization immediately ensued. The tan prisms were filtered off and washed with alcohol giving 2·0 g. (85%) of material which decomposed when heated but had no m. p. up to 300°. Before analysis, the *compound* was recrystallized twice from *tert.*-amyl alcohol (Found, in material dried *in vacuo* at room temperature: C, 32·1; H, 2·9; Br, 58·4. $C_{11}H_{11}O_2Br_3$ requires C, 31·8; H, 2·7; Br, 57·8%). Ultraviolet max. at 290 mμ (ε 4600) in 95% alcohol.

3-*Bromo-5 : 8-dihydro-2-methyl-1 : 4-naphthaquinone.*—The above tribromoquinol (1·0 g.) and sodium iodide (2·0 g.) were refluxed overnight in acetone (8 c.c.), then poured into aqueous sodium thiosulphate, and the whole was extracted twice with ether. The washed extract was oxidized by shaking it with acidified potassium dichromate solution after which the yellow ether layer was separated, washed free from acid with water, dried, and evaporated.

The yellow residue recrystallized from alcohol, from which the *compound* separated in needles, originally yellow, but becoming black when kept. The yield was 500 mg. (82%) and the m. p. 142° (decomp.) after sintering at 137°. The m. p. was unchanged by further recrystallizations (Found, in material dried *in vacuo* at room temperature: C, 52·45; H, 3·8; Br, 31·8. $C_{11}H_9O_2Br$ requires C, 52·1; H, 3·6; Br, 31·6%). Ultraviolet max. at 267 mμ (ε 10,500). When kept, the compound darkens considerably, the m. p. changes, and the absorption begins to resemble that of 3-bromo-2-methyl-1 : 4-naphthaquinone (see below). The maxima of black needles three weeks after preparation were at 245 (ε 7300) and 280 mμ (ε 8000) in 95% alcohol.

Oxidation of the above compound by chromic acid in acetic acid at 90° gave, after dilution with water, filtration, and recrystallization of the yellow solid from alcohol, 3-bromo-2-methyl-1 : 4-naphthaquinone, m. p. 154·5° undepressed on admixture with an authentic specimen. The ultraviolet absorption maxima of this quinone are at 245 (ε 13,800) and 280 mμ (ε 13,200) in 95% alcohol.

2 : 3 : 6 : 7-*Tetrabromo*-2 : 3 : 5 : 6 : 7 : 8-*hexahydro*-2-*methyl*-1 : 4-*naphthaquinone*.—5 : 8-Dihydro-2-methyl-1 : 4-naphthaquinol (1·0 g.) was dissolved in hot acetic acid (10 c.c.) and water (10 c.c.), and treated with bromine (2·8 g.) in acetic acid (1 c.c.). The mixture was boiled for a few seconds and allowed to cool. The *compound* crystallized on cooling as very pale yellow plates (1·7 g., 61%), m. p. 138—139° (decomp.) after sintering at 135°. After two recrystallizations from alcohol, the compound formed colourless plates, m. p. 148—149° (decomp.), after sintering at 135° (Found, in material dried *in vacuo* at 50°: C, 26·7; H, 2·2; Br, 64·3. $C_{11}H_{10}O_2Br_4$ requires C, 26·75; H, 2·0; Br, 64·8%). Ultraviolet max. at 275 mμ (ε 5300) in 95% alcohol. The compound was insoluble in aqueous alkali and was recovered unchanged after being shaken in ether with acidified potassium dichromate solution. Hot acetic acid containing anhydrous sodium acetate appeared to decompose the compound.

6 : 7-*Dibromo*-5 : 6 : 7 : 8-*tetrahydro*-2-*methyl*-1 : 4-*naphthaquinone*.—The above tetrabromo-compound (1·0 g.) and sodium iodide (2·0 g.) were mixed with acetone (20 c.c.). Free iodine was liberated at once. The whole was gently refluxed for 30 min., poured into aqueous sodium thiosulphate, and extracted with ether. The washed, dried, and evaporated extract gave a crystalline residue which recrystallized from alcohol, giving the *compound* (350 mg., 52%) as deep yellow rods, m. p. 72—73° unchanged by further recrystallization from alcohol (Found, in material dried *in vacuo* at room temperature: C, 40·2; H, 3·35; Br, 47·8. $C_{11}H_{10}O_2Br_2$ requires C, 39·5; H, 3·0; Br, 47·8%). Ultraviolet max. at 255 mμ (ε 24,000) in 95% alcohol. The compound decomposed when kept to a material only partly soluble in alcohol and of indefinite m. p. (84° upwards).

When the tetrabromo-compound (3·0 g.) and sodium iodide (9·0 g.) were refluxed for 24 hr. in acetone (140 c.c.), and the resulting mixture was poured into water, a yellow solid separated which darkened rapidly in air. This solid was dissolved in acetic acid (10 c.c.) and treated with a solution of chromic acid in acetic acid, the temperature being kept at 50°. Next morning the dark solution was poured into water, and the yellow crystals which separated were filtered off, washed with water, and dried (yield, 400 mg., 38%; m. p. 105—106°). Recrystallized from alcohol it had m. p. 107—109° alone or mixed with 2-methyl-1 : 4-naphthaquinone.

3 : 6 : 7-*Tribromo*-5 : 6 : 7 : 8-*tetrahydro*-2-*methyl*-1 : 4-*naphthaquinone*.—3 : 6 : 7-Tribromo-5 : 6 : 7 : 8-tetrahydro-2-methyl-1 : 4-naphthaquinol (3·5 g.) was shaken with ether (200 c.c.) and a solution of potassium dichromate (5 g.) and sulphuric acid (2 c.c.) in water (50 c.c.) till no further colour change took place. The yellow ether layer was washed free from acid with water, dried, and evaporated. The yellow residue was recrystallized from toluene–alcohol, giving the *compound* as yellow prisms (2·7 g., 78%), m. p. 141—142° (Found, in material dried *in vacuo* at room temperature: C, 32·3; H, 2·4; Br, 57·2. $C_{11}H_9O_2Br_3$ requires C, 32·0; H, 2·2; Br, 58·1%). Ultraviolet max. at 275 mμ (ε 12,900) in 95% alcohol. The same compound was prepared by the action of hot bromine in acetic acid on the quinol.

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