# Reactions of Indane-1,3-diones with 1,4-Naphthoquinones

By **Katherine Buggle,* John A. Donnelly,** and **Lorcan J. Maher,** Department of Chemistry, University College, Belfield, Dublin 4, Ireland

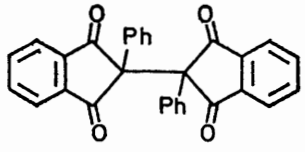
1,4-Naphthoquinones reacted with anticoagulant indane-1,3-diones to yield didehydro-addition products. Those substituted at position 3 by a poor leaving group effected oxidative dimerisation of 2-phenylindane-1,3-dione.

ZALUKAEV and his co-workers have observed that 2-phenylindane-1,3-dione reacts with *p*-benzoquinone in benzene or chloroform to give the didehydro-dimer (I).[1] A similar reaction with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in ethanol has been reported by Becker.[2] Zalukaev and Barsukova [3] later found that 2-phenylindane-1,3-dione reacts with 1,4-naphthoquinone in buffered aqueous acetone to give the didehydro-adduct (II). We have briefly reported [4] that 2-phenylindane-1,3-dione reacts quantitatively with 1,4-naphthoquinone in polar or non-polar solvents to give the didehydro-adduct (II). We now find that 2-phenylindane-1,3-dione with *p*-benzoquinone gives a didehydro-adduct, 2-(benzoquinon-2-yl)-2-phenylindane-1,3-dione, when the solvent is ethanol. These results, which suggest that the course of the reaction depends upon the redox potential of the quinone and at intermediate redox values upon the solvent, led us to examine how electronic and steric factors influence the reaction of indane-1,3-diones with naphthoquinones.

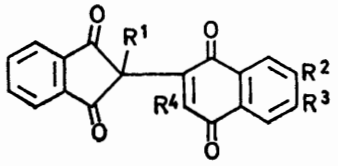
The results in Table 1 show that the naphthoquinones (XII)—(XXII), substituted at position 2 by a leaving group (benzyloxy, acetoxy, or bromo) undergo addition of the indanedione followed by elimination of the leaving group to give the substituted didehydro-adducts (II)—(VII). Only in one case, that of 2-acetoxy-1,4-naphthoquinone (XIII), was the didehydro-adduct (III) formed by addition at the 3-position isolated.

2-Phenylindane-1,3-dione, treated with 2,3-dibromo-1,4-naphthoquinone (XVI) or 2,3-dibromo-6,7-dimethyl-1,4-naphthoquinone (XIX) in either ethanol or benzene solution for 3 days, afforded the didehydro-dimer (I) but, surprisingly, when these reactions were carried out in refluxing ethanol, addition occurred in both cases. The methyl group in menadione (XX) proved to be deactivating and low yields of the didehydro-adduct (VII) and of the didehydro-dimer (I) were isolated. Better yields of the didehydro-adduct (VII) were obtained by using pyridine (*cf.* ref. 4) or by employing 2-bromo-3-methyl-1,4-naphthoquinone (XXI) in place of menadione. Thomson [5] has reported the preparation of 2-phenylthiojuglone in 80% yield by addition of benzenethiol to juglone and in 60% yield by treating benzenethiol with 3-chlorojuglone in the presence of pyridine.

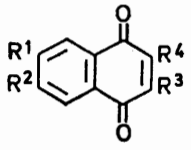
Vitamin $K_1$ also effected the oxidative dimerisation of 2-phenylindane-1,3-dione when the reactants were refluxed in ethanol or pentyl alcohol for long periods. In a control experiment 2-phenylindane-1,3-dione was refluxed in pentyl alcohol for a similar length of time and was recovered unchanged. Addition of pyridine to the vitamin $K_1$ reaction mixture in alcohol did not alter the result.




(I)




(II) $R^1$ = Ph, $R^2$ = $R^3$ = $R^4$ = H
(III) $R^1$ = Ph, $R^2$ = $R^3$ = H, $R^4$ = OAc
(IV) $R^1$ = Ph, $R^2$ = $R^3$ = H, $R^4$ = Br
(V) $R^1$ = Ph, $R^2$ = $R^3$ = Me, $R^4$ = H
(VI) $R^1$ = Ph, $R^2$ = $R^3$ = Me, $R^4$ = Br
(VII) $R^1$ = Ph, $R^2$ = $R^3$ = H, $R^4$ = Me
(VIII) $R^1$ = 4-MeO·$C_6H_4$, $R^2$ = $R^3$ = $R^4$ = H
(IX) $R^1$ = 4-$O_2N$·$C_6H_4$, $R^2$ = $R^3$ = $R^4$ = H
(X) $R^1$ = 1-naphthyl, $R^2$ = $R^3$ = $R^4$ = H
(XI) $R^1$ = $Me_3C$·CO, $R^2$ = $R^3$ = $R^4$ = H




(XII) $R^1$ = $R^2$ = $R^3$ = H, $R^4$ = OBz
(XIII) $R^1$ = $R^2$ = $R^3$ = H, $R^4$ = OAc
(XIV) $R^1$ = $R^2$ = $R^3$ = H, $R^4$ = Br
(XV) $R^1$ = $R^2$ = $R^3$ = $R^4$ = H
(XVI) $R^1$ = $R^2$ = H, $R^3$ = $R^4$ = Br
(XVII) $R^1$ = $R^2$ = Me, $R^3$ = H, $R^4$ = Br
(XVIII) $R^1$ = $R^2$ = Me, $R^3$ = $R^4$ = H
(XIX) $R^1$ = $R^2$ = Me, $R^3$ = $R^4$ = Br
(XX) $R^1$ = $R^2$ = $R^4$ = H, $R^3$ = Me
(XXI) $R^1$ = $R^2$ = H, $R^3$ = Me, $R^4$ = Br
(XXII) $R^1$ = $R^2$ = H, $R^3$ = Me, $R^4$ = phytyl

The results in Table 1 show that the preferred pathway in the range of quinones examined is the addition reaction, but if the addition reaction is made difficult by steric factors then oxidative dimerisation occurs.

Table 2 shows the variation in yield of didehydro-adduct with 1,4-naphthoquinone obtained by varying the addend. 2-(4-Nitrophenyl)indane-1,3-dione and 2-(1-naphthyl)indane-1,3-dione gave excellent yields of

[1] L. P. Zalukaev, V. V. Krivoshein, and G. A. Kharina, *J. Gen. Chem. U.S.S.R.*, 1964, **34**, 2497.
[2] H.-D. Becker, *J. Org. Chem.*, 1965, **30**, 989.
[3] L. P. Zalukaev and L. G. Barsukova, *Zhur. org. Khim.*, 1970, **6**, 2572.
[4] K. Buggle, J. A. Donnelly, and L. J. Maher, *Chem. Comm.*, 1971, 955.
[5] R. H. Thomson, *J. Chem. Soc.*, 1951, 1237.

didehydro-adduct when the reaction was carried out in ethanol but no reaction occurred when the solvent was benzene. If a few drops of base, or even ethanol, were added to these benzene solutions the reactions proceeded giving the didehydro-adducts in good yield. This result supports the view that the reaction proceeds from the enol form of the 1,3-dione (*cf.* ref. 6) and that in benzene solution there is insufficient of the enol form of these two indanediones for the addition reaction to proceed. Zalukaev *et al.*[1] found that 2-(4-nitrophenyl)indane-1,3-dione did not react with *p*-benzoquinone in benzene or chloroform.

TABLE 1

Reaction of 2-phenylindane-1,3-dione with 1,4-naphthoquinones

| | | | Ethanol | | | Benzene | | |
|---|---|---|---|---|---|---|---|---|
| Quinone | $-E_{\frac{1}{2}}$/mV | Time (h) | Didehydro-adduct | % | Didehydro-dimer (I)(%) | Didehydro-adduct | % | Didehydro-dimer (I)(%) |
| (XII) | (140) | 24 | (II) | 98 | | (II) | 83 | |
| (XIII) | 140 | 24 | (II) | 98 | | (II) | 88 | |
| | | | | | | (III) | 11 | |
| (XIV) | 150 | 24 | (II) | 98 | | (II) | 90 | |
| (XV) | 164 | 24 | (II) | 98 | | (II) | 96 | |
| (XVI) | 167 | 72 | | | 79 | | | 61 |
| | | 24 * | (IV) | 94 | | | | |
| (XVII) | 201 | 36 | (V) | 99 | | (V) | 27 | 72 |
| (XVIII) | 220 | 36 | (V) | 98 | | (V) | 79 | 18 |
| (XIX) | 223 | 72 | | | 55 | | | 41 |
| | | 24 * | (VI) | 50 | 10 | | | |
| (XX) | 224 | 72 * | (VII) | 9 | 27 | | | |
| (XXI) | 239 | 72 * | (VII) | 37 | | | | |
| (XXII) | 363 | 100 * | | | 50 | | | |
| | | 100 † | | | 80 | | | |

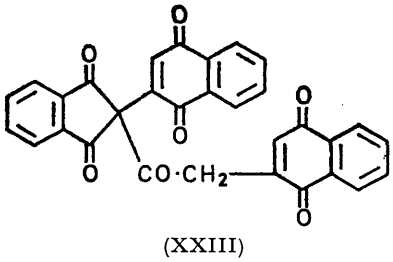
* Reflux temp. (otherwise room temp.). † Pentyl alcohol at reflux temp.

TABLE 2

Reactions of indane-1,3-diones and benzo[*b*]thiophen-3(2*H*)-one 1,1-dioxides with 1,4-naphthoquinone

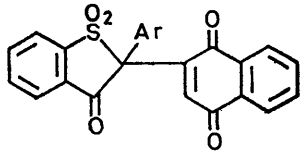
| Addend | Solvent | Time (h) | Temp. | Dehydro-adduct | Yield (%) |
|---|---|---|---|---|---|
| 2-(4-Methoxyphenyl)indane-1,3-dione | Benzene | 24 | R.t.* | (VIII) | 71 |
| | Ethanol | 24 | R.t. | (VIII) | 94 |
| 2-(4-Nitrophenyl)indane-1,3-dione | Benzene | 24 | R.t. | No reaction | |
| | Ethanol | 24 | R.t. | (IX) | 95 |
| 2-(1-Naphthyl)indane-1,3-dione | Benzene | 48 | Reflux | No reaction | |
| | Ethanol | 48 | Reflux | (X) | 90 |
| 2-Acetylindane-1,3-dione | Ethanol | 120 | Reflux | (XXIII) | 36 |
| 2-Pivaloylindane-1,3-dione | Ethanol | 40 | Reflux | (XI) | 27 |
| 2-(4-Nitrophenyl)benzo[*b*]thiophen-3(2*H*)-one 1,1-dioxide | Ethanol | 32 | Reflux | (XXIV) | 78 † |
| 2-Phenylbenzo[*b*]thiophen-3(2*H*)-one 1,1-dioxide | Ethanol | 56 | Reflux | (XXV) | 38 |

* Room temp. † Isolated as the hydroquinone.




(XXIII)

The triketone 2-acetylindane-1,3-dione reacted with 2 equiv. of 1,4-naphthoquinone to form the didehydro-adduct (XXIII). 2-Pivaloylindane-1,3-dione gave a low yield of didehydro-adduct, possibly because of the stabilising effect of hydrogen bonding on the enol form. The benzo[*b*]thiophenone 1,1-dioxides examined are less acidic (*cf.* ref. 7) and were less active in the addition reaction than the corresponding indane-1,3-diones. Both 2-pivaloylindane-1,3-dione and 2-phenylbenzo[*b*]thiophen-3(2*H*)-one 1,1-dioxide were recovered unchanged when refluxed with menadione (XX) in ethanol for 72 h.




(XXIV) Ar = 4-$O_2N{\cdot}C_6H_4$
(XXV) Ar = Ph

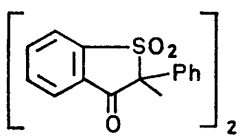
Beringer and Galton [8] reported that treatment of the dimer (I) with base gave 2,3-diphenyl-1,4-naphthoquinone and proposed a mechanism for the reaction. We have found that a similar reaction with the dimer (XXVI) obtained by treatment of 2-phenylbenzo[*b*]-thiophen-3-(2*H*)one 1,1-dioxide with DDQ, gives a compound the analytical and spectroscopic data for

[6] S. E. Fumagalli and C. H. Eugster, *Helv. Chim. Acta*, 1971, **54**, 959.

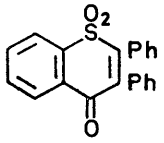
[7] J. G. Lombardino and E. H. Wiseman, *J. Medicin. Chem.*, 1970, **13**, 206.

[8] F. M. Beringer and S. A. Galton, *J. Org. Chem.*, 1963, **28**, 3250.

which are consistent with the structure of 3-phenyl-1-thioflavone 1,1-dioxide (XXVII).



(XXVI)



(XXVII)

## EXPERIMENTAL

I.r. spectra were obtained for chloroform solutions with a Perkin-Elmer 700 spectrometer and n.m.r. spectra were recorded for solutions in [$^2$H]chloroform with a Perkin-Elmer R12 spectrometer operating at 60 MHz (tetramethylsilane as internal standard). U.v. spectra were measured for solutions in methanol with a Perkin-Elmer 124 spectrometer. Merck Kieselgel $PF_{254+366}$ was used for thin (t.l.c.) and preparative layer chromatography (p.l.c.).

The 2-substituted indane-1,3-diones,[9,10] benzo[*b*]thiophen-3(2*H*)-one 1,1-dioxides,[11,12] and quinones[13,14] used were prepared by previously described methods. Redox values were obtained from the literature or calculated by the method described by Currie.[15]

*Reaction of 2-Phenylindane-1,3-dione with p-Benzoquinone.*—A solution of *p*-benzoquinone (216 mg, 0·002 mol) in ethanol (5 ml) was added to a solution of 2-phenylindane-1,3-dione (222 mg, 0·001 mol) in ethanol (5 ml) and the mixture was kept at room temperature for 24 h. On partial evaporation of the solvent 2-(*benzoquinon-2-yl*)-2-*phenylindane-1,3-dione* separated in needles. A further quantity of the didehydro-adduct was obtained by p.l.c. of the mother liquor. The combined product (314 mg, 95%) had m.p. 156—157° (ethanol) (Found: C, 76·4; H, 3·8. $C_{21}H_{12}O_4$ requires C, 76·8; H, 3·7%), $\nu_{max.}$ ($CHCl_3$) 1745w, 1710s, and 1660s cm$^{-1}$; τ 3·65 (1H, m), 3·14 (2H, m), and 1·78—2·6 (9H, m).

*Reactions of Indane-1,3-diones and Benzo*[b]*thiophen-3*(2H)*-one 1,1-Dioxides with 1,4-Naphthoquinone* (*Tables 1 and 2*).—A solution of 1,4-naphthoquinone (1 mmol) in ethanol (5 ml) was added to a solution of the addend (0·5 mmol) in ethanol (5 ml, or the minimum required to effect dissolution). Analytical data for the didehydro-adducts formed are given in Table 3. The u.v. spectra (Table 4) of the didehydro-adducts are in agreement with the proposed structures. The i.r. spectra of the didehydro-adducts show the typical carbonyl absorptions at 1710 and 1746 cm$^{-1}$ of the indane-1,3-dione structure as well as absorption due to the quinone system at 1665 cm$^{-1}$. All n.m.r. signals occurred in the aromatic region except those of substituent methyl groups.

*Dimerisation of 2-Phenylbenzo*[b]*thiophen-3*(2H)*-one 1,1-Dioxide.*—A solution of DDQ (227 mg) in methanol (5 ml) was added to a solution of 2-phenylbenzo[*b*]thiophen-3(2*H*)-one 1,1-dioxide (534 mg) in methanol (10 ml) under nitrogen and the mixture was stirred for 24 h. The resulting precipitate crystallised from ethanol as *bis*-(2,3-*dihydro*-3-*oxo*-2-*phenylbenzo*[b]*thiophen*-2-*yl*) *tetra*-S-*oxide* (XXVI) (424 mg, 80%), m.p. 221—225° (Found: C, 65·0; H, 3·8; S, 12·5. $C_{28}H_{18}O_6S_2$ requires C, 65·4; H, 3·5; S, 12·4%), $\lambda_{max.}$ 248 nm (log ε 4·36); $\nu_{max.}$ 1720 and 1320 cm$^{-1}$; τ 1·59—2·97 (m).

*3-Phenyl*(*thioflavone*) *1,1-Dioxide* (XXVII).—A mixture of the didehydro-dimer (XXVI) (200 mg) in dioxan (10 ml) and aqueous N-sodium hydroxide (10 ml) was refluxed overnight under nitrogen; the solution was then distilled to *ca.* 5 ml. The residue was diluted with water (100 ml), acidified with dilute hydrochloric acid (10%), and extracted with chloroform. The chloroform solution was dried and the solvent was distilled off. P.l.c. of the residue yielded the *dioxide* (XXVII), which crystallised from chloroform–light petroleum (b.p. 60—80°) (50 : 50) in microcrystals (103 mg), m.p. 133—135° (Found: C, 72·6; H, 4·2; S, 9·4. $C_{21}H_{14}O_3S$ requires C, 72·8; H, 4·1; S, 9·2%); $\nu_{max.}$ 1700 cm$^{-1}$, τ 1·76—2·75 (m).

TABLE 3

Analytical data

| Compound † | M.p. (°C) | Found (%) C | H | Formula | Reqd. (%) C | H |
|---|---|---|---|---|---|---|
| (II) | 290—292 [a] | | | | | |
| (III) | 253—255 | 74·6 | 3·8 | $C_{27}H_{14}O_6$ | 74·3 | 3·8 |
| (IV) | 230—223 | 65·9 | 2·9 | $C_{25}H_{13}BrO_4$ [b] | 65·7 | 2·8 |
| (V) | 243—245 | 80·3 | 4·7 | $C_{27}H_{18}O_4$ | 79·8 | 4·5 |
| (VI) | 248—251 | 66·9 | 3·6 | $C_{27}H_{17}BrO_4$ [c] | 66·8 | 3·5 |
| (VII) | 196—197 | 79·8 | 4·3 | $C_{26}H_{16}O_4$ | 79·6 | 4·1 |
| (VIII) | 210 [d] | | | | | |
| (IX) | 252 [e] | | | | | |
| (X) | 264—265 | 80·9 | 3·7 | $C_{29}H_{16}O_4$ | 81·3 | 3·8 |
| (XI) | 172—174 [f] | 74·9 | 4·3 | $C_{24}H_{18}O_5$ | 74·6 | 4·7 |
| (XXIII) | 181—183 | 74·4 | 3·5 | $C_{31}H_{16}O_7$ | 74·4 | 3·2 |
| (XXIV) | 195—197 | 63·1 | 3·2 | $C_{24}H_{13}NO_7S$ [g] | 62·7 | 2·9 |
| (XXV) | 278—281 | 69·8 | 3·6 | $C_{24}H_{14}O_5S$ [h] | 69·6 | 3·4 |

† Recryst. from ethanol.

[a] Ref. 4 gives m.p. 308°. [b] Found: Br, 17·5. Required: 17·3%. [c] Found: Br, 16·3. Required: 16·5%. [d] Ref. 4 gives m.p. 210—211°. Ref. 4 gives m.p. 251°. [f] Recryst. from ethanol–water. [g] Found: N, 2·8; S, 7·0. Required: N, 3·0; S, 7·0%. [h] Found: S, 7·6. Required: 7·7%.

TABLE 4

U.v. spectra of adducts

| Product | $\lambda_{max.}$/nm (log ε) |
|---|---|
| (II) | 227 (4·63), 241 (4·52), 246 * (4·52), 252 * (4·44) |
| (III) | 224 (4·65), 240 * (4·53), 244 * (4·52), 250 * (4·48) |
| (IV) | 225 (4·72), 247 (4·48), 253 (4·45), 275 * (4·11) |
| (V) | 227 (4·51), 253 (4·35), 260 (4·31) |
| (VI) | 220 (4·64), 247 (4·50), 253 * (4·48), 282 * (4·00) |
| (VII) | 227 (4·67), 246 (4·53), 252 * (4·50), 268 * (4·19) |
| (VIII) | 216 (4·67), 240 (4·59) |
| (IX) | 230 (4·64), 247 (4·62), 253 (4·61) |
| (X) | 220 (4·83), 245 (4·54), 252 * (4·50), 287 (4·11) |
| (XXIII) | 224 (4·81), 243 (4·80), 252 * (4·66) |
| (XI) | 223 (4·58), 242 (4·65), 252 * (4·44) |
| (XXIV) | 252 (4·38) |
| (XXV) | 257 (4·41) |

* Shoulder.

[2/2348 *Received*, 16*th October*, 1972]

[9] J. C. Godfrey and R. A. Barnes, *J. Amer. Chem. Soc.*, 1958, **80**, 3902.
[10] L. B. Kilgore, J. H. Ford, and W. C. Wolfe, *Ind. Eng. Chem.*, 1942, **34**, 494.
[11] A. Cohen and S. Smiles, *J. Chem. Soc.*, 1930, 406.
[12] W. B. Price and S. Smiles, *J. Chem. Soc.*, 1928, 2858.
[13] E. F. Pratt, R. W. Luckenbaugh, and R. L. Erickson, *J. Org. Chem.*, 1954, **19**, 176.
[14] L. F. Fieser, D. M. Bowen, W. P. Campbell, E. M. Fry, and M. D. Gates, *J. Amer. Chem. Soc.*, 1939, **61**, 1926.
[15] D. J. Currie and H. L. Holmes, *Canad. J. Chem.*, 1966, **44**, 1027.