o-Quinonoid Compounds. Part V.[1] Derivatives of 2,3-Naphthoquinone Dimethide

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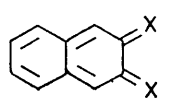
The synthesis of (3-benzoyl-2-naphthyl)phenylacetic acid (7; R = H) incorporating an improved synthesis of 2,2-dihydroxybenz[*f*]indene-1,3-dione is described. In boiling acetic anhydride the acid (7; R = H) is partly dehydrated to 1,4-diphenylnaphtho[2,3-*c*]pyran-3-one (5), which can be trapped with dimethyl maleate, dimethyl fumarate, or *N*-phenylmaleimide. With dimethyl maleate the *exo*-adduct is formed preferentially. 1,4-Diphenylbenz[*g*]isoquinolin-3-ol is formed by reaction of the ester (7; R = Me) with liquid ammonia. It exists predominantly as the lactim tautomer in ethanol.

2,3-NAPHTHOQUINONE (1; X = O) is unknown and its 1,4-diphenyl derivative is a highly reactive intermediate which can be trapped only at low temperatures.[2] A few compounds containing this bond structure stabilised by incorporation into an aromatic system and/or by phenyl conjugation have been prepared or generated as reactive intermediates. These include the furan (2) and the thiophen (3), which are isolable,[3] the isoindole (4) and its 1-phenyl derivative, which have been characterised as



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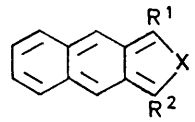
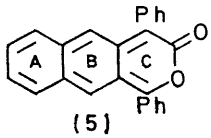


(2) X = O, $R^1 = R^2$ = Ph
(3) X = S, $R^1 = R^2$ = Ph
(4) X = NH, $R^1 = R^2$ = H



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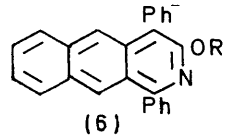

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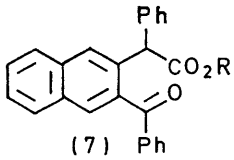

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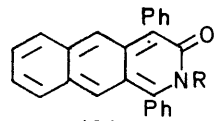

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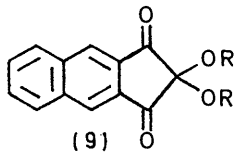

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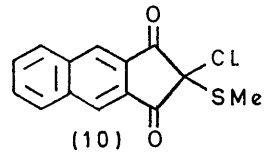

(10)

their Diels–Alder adducts,[4] and the 2,3-naphthoquinone dimethide (1; X = CH_2) [5] and its diphenyl derivatives,[3,6] which are reactive intermediates.

Attempts to prepare 1,4-diphenylnaphtho[2,3-*c*]pyran-3-one (5) were encouraged by the stability of 1,4-diphenyl-2-benzopyran-3-one, which appears to be greater than that of 1,3-diphenylbenzo[*c*]furan.[7] Our interest centred on the cycloaddition reactions of compound (5), since preferred *exo*-addition of dienophiles to benz[*f*]isoindole [4] and 1,4-diphenyl-2,3-naphthoquinone [8] has been observed. Moreover the reduced Diels–Alder reactivity associated with the presence of the ring-C diene system in a six-membered ring [7] might favour a competing addition of dienophiles to the ring-B diene system, as observed in the Diels–Alder reactions of anthracene. Further the 14 π-electron nitrogen analogue, 1,4-diphenylbenz[*g*]isoquinolin-3-ol (6; R = H), might be accessible through the naphthopyran (5) or the ester (7; R = Me). This if so would enable the tautomeric equilibrium (6; R = H) ⇌ (8; R = H) to be investigated and the results compared with those for the isoquinolin-3-ol system.[9,10]

By analogy with earlier work we sought to prepare the pyrone (5) by dehydration of (3-benzoyl-2-naphthyl)-phenylacetic acid (7; R = H). Preparation of the latter required an efficient synthesis of 2,2-dihydroxybenz[f]indene-1,3-dione (9; R = H), previously available in only 18% yield.[11] Compound (9; R = H) was obtained in 46% yield by a sequence originally developed for the preparation of ninhydrin from dimethyl phthalate.[12] Condensation of dimethyl sulphoxide with dimethyl naphthalene-2,3-dicarboxylate and Pummerer rearrangement of the product gave the chloro-thioether (10). Hydrolysis of compound (10) then gave the ninhydrin analogue (9; R = H). Conversion of this into its dimethyl ether (9; R = Me) [13] could only be accomplished in high yield (67%) on a small scale (150 mg). Treatment of the ether (9; R = Me) with an excess of phenylmagnesium bromide gave the desired dihydroxy-acetal (11), which was expected [7] to give the acid (7; R = H) on acidic hydrolysis (HCl–HOAc). However this reaction proceeded poorly at 20°; the keto-acid (7; R = H) was obtained together with an equal quantity of 1,3-dihydroxy-1,3-diphenylbenz[*f*]-

[1] Part IV, J. M. Holland and D. W. Jones, *J. Chem. Soc.* (*C*), 1971, 608.
[2] D. W. Jones and R. L. Wife, *Chem. Comm.*, 1970, 1086.
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[4] J. E. Shields and J. Bornstein, *Chem. and Ind.*, 1967, 1404.
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[6] M. P. Cava, B. Hwang, and J. P. Van Meter, *J. Amer. Chem. Soc.*, 1963, **85**, 4031.
[7] J. M. Holland and D. W. Jones, *J. Chem. Soc.* (*C*), 1970, 530.
[8] D. W. Jones and R. L. Wife, unpublished results.
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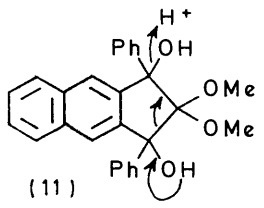
indan-2-one. When the reaction was conducted at reflux temperature compound (7; R = H) was isolable in only low yield owing to contamination by coloured impurities. Accordingly, other methods for the conversion of the ether (9; R = Me) into the acid (7; R = H) were sought. A solution of the dihydroxy-acetal (11) in trifluoroacetic acid, kept at 20° for 2 h, gave the methyl ester (7; R = Me) in 81% yield. This reaction was conveniently followed by n.m.r. spectroscopy. A likely mechanism for the reaction involves a retro-Prins reaction (11; arrows) to give the keten acetal (12), which is then converted (12; arrows) into the ester (7; R = Me). When this reaction was conducted in deuteriotrifluoroacetic acid the resulting ester was deuteriated at the doubly benzylic carbon atom, as indicated by the absence of resonance at τ 4·12 ($CDCl_3$). Alkaline hydrolysis of the ester (7; R = Me) gave the acid (7; R = H) in quantitative yield; the overall yield from dimethyl naphthalene-2,3-dicarboxylate was 14%. The occurrence of a rearrangement involving phenyl migration in the reaction of the ether (9; R = Me) with acid was excluded by oxidation of the acid (7; R = H) to 2,3-dibenzoylnaphthalene.



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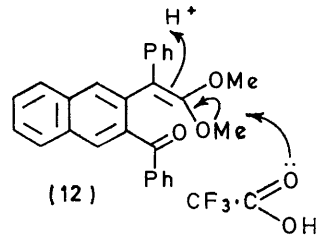

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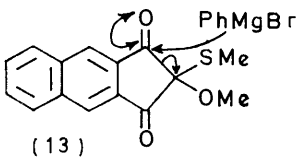

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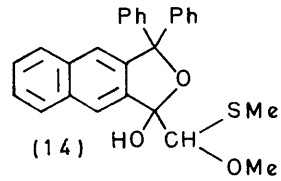

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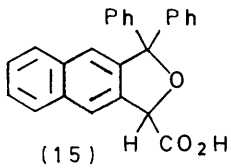

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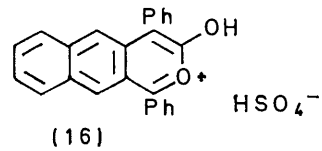
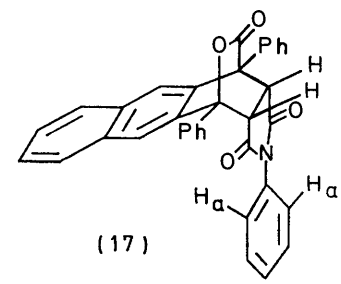


(16)

An attempt was made to simplify the preparation of the acid (7; R = H) and avoid the tedious methylation of compound (9; R = H). In boiling methanol the chloro-thioether (10) gave the mixed acetal (13) in high yield. However this compound was not an appropriate substitute for the acetal (9; R = Me); the β-diketone system was cleaved (13; arrows) on treatment with phenylmagnesium bromide. Subsequent reaction with the Grignard reagent and work-up gave the hemiacetal (14). On acidic hydrolysis compound (14) gave the acid (15). The ability of a sulphur atom to stabilise a neighbouring carbanion presumably accounts for the difference in behaviour of compounds (9; R = Me) and (13) in the Grignard reaction.

Dissolution of the keto-acid (7; R = H) in concentrated sulphuric acid gave a deep blue colour attributed to the salt (16). However on addition of water the blue colour faded instantly and the acid (7; R = H) was recovered. Unlike 1,4-diphenyl-2-benzopyran-3-one,[7] the linearly annulated derivative (5) was presumably too easily hydrolysed to be prepared in this way. An attempt to dehydrate the acid (7; R = H) by treatment with dicyclohexylcarbodi-imide * produced no colour, and no adduct of (5) could be isolated in the presence of *N*-phenylmaleimide.

The pyrone (5) was produced by dehydration of the acid (7; R = H) in boiling acetic anhydride. A deep blue colour ($\lambda_{max.}$ *ca.* 700 nm) developed after a few minutes boiling. This colour was rapidly discharged on addition of dienophiles.



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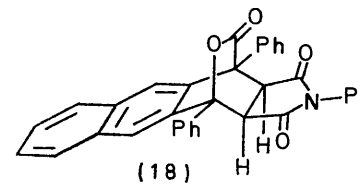

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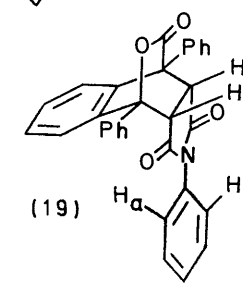

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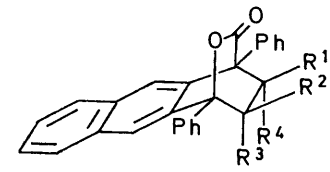

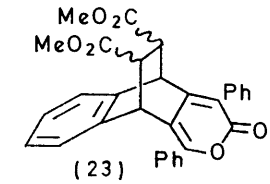

(23)

(20) $R^1 = R^3 = CO_2Me$, $R^2 = R^4 = H$
(21) $R^3 = R^4 = CO_2Me$, $R^1 = R^2 = H$
(22) $R^1 = R^2 = CO_2Me$, $R^3 = R^4 = H$

When the keto-acid and *N*-phenylmaleimide were heated in boiling acetic anhydride the initial colour faded during 1·25 h and a 2 : 1 mixture of the adducts (17) and (18) was isolated in 72% yield. The configuration of the *endo*-adduct follows from the n.m.r.

* A yellow solution of 1-methyl-2-benzopyran-3-one is readily prepared by heating *o*-acetylphenylacetic acid with dicyclohexylcarbodi-imide. We thank Professor C. W. Rees for suggesting this method.

spectrum. In addition to signals for aromatic protons at τ 1·7—3·3, and an apparent singlet for the methine protons at 5·5, the signals for the aromatic protons (H_a) appear as a multiplet at 3·8—4·2. The latter are shielded by the naphthalene system [14] and resonate 0·5 p.p.m. to higher field than the protons H_a in the related adduct (19), which are shielded by a phenylene ring. The shielded aromatic protons in these and related adducts have been unequivocally identified by deuterium-labelling experiments.[15] As expected the n.m.r. spectrum of the *exo*-adduct (18) shows no shielded aromatic protons, whereas the methine protons are relatively shielded. They appear as an AB system centred at τ 5·82.

Addition of *N*-phenylmaleimide to 1,4-diphenyl-2-benzopyran-3-one under similar conditions (refluxing xylene) gave *endo*- (77%) and *exo*- (23%) adducts; addition to 2-benzopyran-3-one and its derivatives gave only *endo*-adducts.[16] To exclude the possibility that the increased *exo*-addition observed here arose by a mechanism not involving the pyrone (5),[16] the stereospecificity of the addition to dimethyl maleate and dimethyl fumarate was tested. In the presence of the more reactive dimethyl fumarate [17] the blue colour attributed to compound (5) faded rapidly (2·5 h) as the adduct (20) was formed. With dimethyl maleate the reaction proceeded at an acceptable rate in the presence of a large excess of dienophile and gave the *endo*- (21) (12·5%) and the *exo*-adduct (22) (22%). The assignment of stereochemistry is based in part on the position and appearance of the methine proton resonance in the n.m.r. spectrum (*cf.* the *N*-phenylmaleimide adducts). This abrogation of Alder's rule of preferred *endo*-addition * is the subject of further study. It is apparently associated with a six-membered ring diene component with terminal phenyl substituents as well as with a lack of rigidity in the dienophile. Under these circumstances secondary orbital interactions favouring the *endo*-transition state [18] may compete unfavourably with steric effects which seem to favour the *exo*-transition state.[8]

The reaction of compound (5) with dimethyl fumarate gave, in addition to the adduct (20), a non-crystalline and chromatographically inseparable mixture of two compounds which are tentatively assigned the gross structure (23). The mass spectrum shows a molecular ion at *m/e* 492, the u.v. spectrum [$\lambda_{max.}$ (EtOH) 332 nm] is similar to that of 3,6-diphenyl-2-pyrone,[19] and the n.m.r. spectrum (Experimental section) is appropriate for a mixture of two isomers of structure (23). A similar but different mixture was formed in the addition of dimethyl maleate to compound (5). The factors responsible for predominant *exo*-addition of these dienophiles to ring C of compound (5) presumably also lead to reduced ring-C diene reactivity and so allow a competing addition to the ring-B diene.

Synthesis and Tautomerism of 1,4-*Diphenylbenz*[g]*isoquinolin*-3-*ol*.—When the methyl ester (7; R = Me) reacted with liquid ammonia the benz[*g*]isoquinolin-3-ol (6; R = H) was formed. The u.v. spectrum of the product in ethanol shows long wavelength absorption at 433 nm (ε 6690), and only weak absorption at longer wavelength (ε 340 at 560 nm). The tautomerism between the fully aromatic lactim (6; R = H) and the naphthoquinonoid lactam (8; R = H) was investigated by comparison with the u.v. spectra of the fixed methyl derivatives (6; R = Me) and (8; R = Me). Treatment of compound (6; R = H) with diazomethane gave mainly the *O*-methyl derivative (6; R = Me), $\lambda_{max.}$ (EtOH) 434 nm (ε 7160). The *N*-methyl derivative (8; R = Me) was prepared (83%) by the reaction of the methyl ester (7; R = Me) with methylamine and treatment of the crude product with acetic acid; it showed $\lambda_{max.}$ (EtOH) 560 nm (ε 4755). Thus in the tautomeric equilibrium (6; R = H) ⇌ (8; R = H) the lactim form is strongly favoured (*ca.* 90%). The lactim is only slightly favoured for 1,4-diphenylisoquinolin-3-ol.[9] The effect of increasing linear annulation on tautomeric equilibrium is clearly illustrated by the series 2-pyridone, isoquinolin-3-ol, benz[*g*]isoquinolin-3-ol. For the first compound the lactam is overwhelmingly favoured,[20] for the second the equilibrium is finely balanced between the two tautomers and is dependent on both substitution and solvent,[9,10] and for 1,4-diphenylbenz[*g*]isoquinolin-3-ol the lactim tautomer is strongly favoured even in a polar solvent.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. Unless specified, i.r. spectra refer to Nujol mulls, u.v. spectra to ethanolic solutions, and n.m.r. spectra to solutions in deuteriochloroform measured with a Varian A60A spectrometer. Mass spectra were obtained on an A.E.I. MS902 instrument. 'Petroleum' refers to light petroleum (b.p. 60—80°), and chromatography on silica to short column [21] chromatography over Kieselgel G (Merck). The term 'isolation of acids in the usual way' refers to washing an ether solution with saturated sodium hydrogen carbonate solution, acidification of the aqueous layer with hydrochloric acid (2N), and extraction into ether.

2-*Chloro*-2-*methylthiobenz*[f]*indene*-1,3-*dione* (10).—Sodium methoxide (4·51 g, 0·0836 mol) was suspended in anhydrous dimethyl sulphoxide (50 ml) under nitrogen. The suspension was stirred and dimethyl naphthalene-2,3-dicarboxylate (5·00 g, 0·0205 mol) in anhydrous dimethyl sulphoxide (50 ml) was added dropwise during 10 min. The mixture was stirred for 2·0 h and then excess of solvent

* Adducts (21) and (22) have been shown not to isomerise in boiling acetic anhydride during 1·3 h; thus the preferred mode of addition is due to kinetic and not thermodynamic control.

[14] L. M. Jackman and S. Sternhell, 'Nuclear Magnetic Resonance in Organic Chemistry,' Pergamon, Oxford, 1969, p. 96.
[15] D. W. Jones and G. Kneen, *Chem. Comm.*, 1971, 1356.
[16] J. M. Holland and D. W. Jones, *J. Chem. Soc.* (*C*), 1970, 536.
[17] J. Sauer, *Angew. Chem. Internat. Edn.*, 1967, **6**, 25.
[18] R. Hoffmann and R. B. Woodward, 'The Conservation of Orbital Symmetry,' Verlag Chemie, Weinheim, 1970, p. 145.
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was removed by vacuum distillation (48—50° at 0·1 cmHg). To the yellow residue were added ether (100 ml) and ice–water (100 ml) with stirring. The yellow aqueous layer was added dropwise to hydrochloric acid (6N; 100 ml) with stirring. The white precipitate was dissolved as completely as possible in methylene chloride (400 ml), the solution was filtered to remove naphthalene 2,3-dicarboxylic acid, and the methylene chloride solution was washed with water, and dried (Na_2SO_4). Evaporation left the *chlorothioether* (10) (2·76 g, 49%), m.p. 155—158° (from benzene–petroleum) (Found: C, 61·05; H, 3·5; Cl, 12·4; S, 11·65. $C_{14}H_9ClO_2S$ requires C, 60·8; H, 3·3; Cl, 12·85; S, 11·6%), $\nu_{max.}$ 1740, 1710, 1240, 1195, 920, 845, and 770 cm^{-1}, $\lambda_{max.}$ (cyclohexane) 234, 264sh, 272, 301, 313, 329sh, 343sh, and 361 nm (ε 13,225, 46,960, 70,930, 6615, 6615, 4500, 2205, and 1440), τ 1·3 (2H, s, H-4, H-9), 1·5—2·2 (4H, m, H-5, -6, -7, -8), and 7·48 (3H, s), *m/e* 241 (*M* − Cl), 226, 216, 208, 198, and 195 (97, 21, 12, 21, 47, and 100%).

2,2-Dihydroxybenz[f]*indene-1,3-dione* (9; R = H).—2-Chloro-2-methylthiobenz[*f*]indene-1,3-dione (10) (2·76 g) was added in portions to water (100 ml) and peroxide-free dioxan (10 ml) at 100°, and the mixture was boiled under reflux for 18 h. The hot solution was then filtered, the filtrate cooled to 5°, and the product (9; R = H) collected as plates (2·12 g, 93%), m.p. 276—280° (lit.,[11] 279—282°).

2,2-Dimethoxybenz[f]*indene-1,3-dione* (9; R = Me).—This reaction was performed on several batches (36 × 150 mg) of compound (9; R = H). Any increase in scale reduced the yield considerably.

Mixtures of compound (9; R = H) (150 mg, 0·66 mmol), methyl iodide (1·64 g, 0·0115 mol), and silver oxide * (0·355 g, 0·0016 mol) in dimethylformamide (8 ml) and water (0·24 g) were shaken vigorously at 20° for 4·0 h; the mixtures were diluted with chloroform, combined, filtered through Celite, and evaporated to dryness to give a green solid. The crude product in benzene was filtered through a short column of neutral alumina (Woelm, grade III) to give the *ether* (9; R = Me) (3·44 g, 67%), m.p. 158—160° (from methanol) (Found: C, 70·35; H, 4·85. $C_{15}H_{12}O_4$ requires C, 70·4; H, 4·8%), $\nu_{max.}$ 1735, 1715, 1700, 1625, 1605, 1590, 1155, 1050, and 770 cm^{-1}, $\lambda_{max.}$ 224, 272, 316, and 360 nm (ε 14,650, 70,730, 3200, and 1680), τ 1·33 (2H, s, H-4, H-9), 1·65—2·25 (4H, m, H-5, -6, -7, -8), and 6·2 (6H, s), *m/e* 256 (*M*), 224, 212, and 196 (29, 3, 100, and 10%).

1,3-Dihydro-2,2-dimethoxy-1,3-diphenylbenz[f]*indene-1,3-diol* (11).—The ether (9; R = Me) (1·76 g, 0·0068 mol) in benzene (30 ml) was added dropwise to phenylmagnesium bromide [from bromobenzene (4·32 g, 0·0275 mol) and magnesium (0·67 g, 0·0279 g atom)] in ether (75 ml) and benzene (20 ml) at 20° under nitrogen. The mixture was boiled under reflux for 1·5 h and cooled; a saturated aqueous solution of ammonium chloride (100 ml) was added. The organic layer was separated, washed with water (100 ml), and dried (Na_2SO_4). Evaporation gave a red oil which crystallised from methanol to give the *dihydroxy-acetal* (11) (1·65 g, 57%), m.p. 178—179° (from benzene–petroleum) (Found: C, 77·9; H, 6·0. $C_{27}H_{24}O_4$ requires C, 78·25; H, 6·3%), $\nu_{max.}$ 3500, 3410, 1610, 1055, 760, and 710 cm^{-1}, $\lambda_{max.}$ 232, 265, 275, 285, and 295 nm (ε 91,380, 3970, 5000, 5000, and 3500), τ 1·95—2·70 (16H, m, aromatic), 5·69 (2H, s, OH, exch. D_2O), and 7·01 (6H, s), *m/e* 412 (*M*), 394, 379, and 351 (5, 100, 43, and 39%).

* The quality of the silver oxide is critical: freshly prepared material adsorbed much of the product and it was necessary to use older and less active silver oxide.

Acidic Hydrolysis of the Dihydroxy-acetal (11).—Compound (11) (100 mg), acetic acid (12·5 ml), concentrated hydrochloric acid (6·3 ml), and water (6·3 ml) were kept at 20° for 7 days. The solvent was removed at 40° and 0·1 mmHg and the solid was taken into ether; the solution was washed with water and dried (Na_2SO_4). Chromatography on silica (40 g) and elution with benzene–ether (7 : 3) gave *1,3-dihydro-1,3-dihydroxy-1,3-diphenylbenz*[f]*inden-2-one* (32 mg, 36%), m.p. 222—230° (from benzene–petroleum) (Found: C, 81·95; H, 4·95. $C_{25}H_{18}O_3$ requires C, 81·90; H, 4·9%), $\nu_{max.}$ 3420, 3350, 1775, 1610, 1010, 895, 760, and 750 cm^{-1}, τ [$(CD_3)_2SO$] 1·86 (2H, s, H-4, H-9), 1·82—2·50 (4H, m, H-5, -6, -7, -8), 2·91 (10H, s, Ph), and 3·24 (2H, s, OH, exch. D_2O), *m/e* 366 (*M*), 336, 319, and 306 (0·45, 20, 100, and 12·5%).

Continued elution, with benzene–ether (1 : 1), gave the keto-acid (7; R = H) (38 mg, 43%) as an oil, τ 1·57—1·82 (1H, s, OH, exch. D_2O), 1·80—2·80 (16H, m, aromatic), and 4·12 (1H, s, benzylic), $\nu_{max.}$ 1710, 1660, 1290, 760, 730, 710, and 695, $\nu_{max.}$ (benzene film) 3500—2800, 1700, 1655, 1290, and 690 cm^{-1}, *m/e* 366 (*M*), 348, 320, 304, and 291 (0·8, 41, 100, 9, and 18%), *m** 294·5 (348 ⟶ 320).

Conversion of the Dihydroxy-acetal (11) *into Methyl* (3-*Benzoyl-2-naphthyl*)*phenylacetate* (7; R = Me).—Compound (11) (400 mg) was dissolved in trifluoroacetic acid (2·0 ml) to give a deep blue-green solution, which was kept at 20° for 1·5 h. The solution was diluted with water (50 ml) and extracted with chloroform (3 × 50 ml). The extracts were combined, washed with sodium hydrogen carbonate solution and water, and dried (Na_2SO_4); evaporation left an orange solid which crystallised on trituration with benzene, giving the *methyl ester* (7; R = Me) (147 mg, 41%). The mother liquor was chromatographed on silica (30 g). Elution with benzene gave more methyl ester (145 mg, 40%), m.p. 145—148° (from benzene–petroleum) (Found: C, 82·25; H, 5·35. $C_{26}H_{22}O_3$ requires C, 82·1; H, 5·3%), $\nu_{max.}$ 1730, 1660, 1605, 1295, 1205, 1180, 915, 760, 750, and 705 cm^{-1}, $\nu_{max.}$ ($CHBr_3$) 1733 and 1658 cm^{-1}, $\lambda_{max.}$ 224, 255, 283, and 338 nm (ε 58,000, 27,000, 9045, and 1570), τ 1·90—2·65 (16H, m, aromatic), 4·12 (1H, s, benzylic), and 6·3 (3H, s), *m/e* 380 (*M*), 348, 320, 291, and 243 (2, 45, 100, 18, and 20%), *m** 294·5 (348 ⟶ 320).

(3-*Benzoyl-2-naphthyl*)*phenylacetic Acid* (7; R = H).—The methyl ester (7; R = Me) (400 mg) was dissolved in purified ethanol (200 ml) and sodium hydroxide (50 mg) was added. The solution was stirred under nitrogen at 20° overnight, neutralised with dilute hydrochloric acid, and concentrated to small volume. Isolation of the acid in the usual way afforded the keto-acid in quantitative yield, identical to material prepared previously (i.r. spectrum).

2-Methoxy-2-methylthiobenz[f]*indene-1,3-dione* (13).—The dione (10) (800 mg) was partially dissolved in dry methanol (25 ml) and the solution boiled under reflux under nitrogen for 4·0 h. Evaporation afforded the *thioacetal* (13) (700 mg, 87%), m.p. 141—144° (from chloroform–methanol) (Found: C, 66·4; H, 4·5; S, 11·65. $C_{15}H_{12}O_3$ requires C, 66·2; H, 4·4; S, 11·75%), $\nu_{max.}$ 1740, 1710, 1625, 1350, 1040, 765, and 760 cm^{-1}, $\lambda_{max.}$ (cyclohexane) 238, 261sh, 269, 295, 311, 328, 343, and 358 nm (ε 14,350, 52,430, 82,790, 7950, 8170, 5520, 2320, and 1545), τ 1·38 (2H, s, H-4, H-9), 1·65—2·35 (4H, m, H-5, -6, -7, -8), 6·08 (3H, s), and 7·67 (3H, s), *m/e* 272 (*M*), 257, 229, 226, 213, and 197 (70, 5, 100, 28, 51, and 28%).

Reaction of the Thioacetal (13) *with Phenylmagnesium Bromide.*—The thioacetal (13) (1·0 g, 0·00368 mol) in dry

benzene (10 ml) was added dropwise to phenylmagnesium bromide [from bromobenzene (2·31 g, 0·01472 mol) and magnesium (0·358 g, 0·01472 g atom)] in benzene (15 ml) and ether (20 ml). The solution was stirred at 20° under nitrogen for 3·6 h, boiled under reflux for a further 2·4 h, and allowed to cool. The mixture was diluted with ether (200 ml), washed with saturated ammonium chloride solution, and extracted with further portions of ether (100 ml); the ether extract was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure to give the crude product. Chromatography on silica (100 g) with benzene–ether (12 : 1) as eluant was unsuccessful, but the mixture was separated on grade III neutral alumina (Woelm) with benzene–petroleum (4 : 1) to give 1,3-*dihydro*-1-[*methoxy*(*methylthio*)*methyl*]-3,3-*diphenylnaphtho*-[c]*furan*-1-*ol* (14) (0·690 g, 46%), m.p. 84—86° (from benzene–petroleum) (Found: C, 75·75; H, 6·05. $C_{27}H_{24}O_3S$ requires C, 75·8; H, 5·6%), $\nu_{max.}$ 3470, 1605, 1185, 1100, 1040, 760, and 710 cm^{-1}, $\lambda_{max.}$ (cyclohexane) 231, 253, 263, 274, 284, and 294 nm (ε 71,350, 5350, 4760, 4760, 4760, and 3270), τ 1·8—2·8 (16H, m), 5·3 (0·67H, s) and 5·42 (0·33H, s), 5·50—5·75 (1H, s, OH, exch. D_2O), 6·49 (1H, s) and 6·67 (2H, s), and 7·83 (2H, s) and 8·05 (1H, s), *m/e* 410 ($M - H_2O$), 395, 367, 363, 320, and 319 (43, 41, 2, 97, 100, and 88%). The n.m.r. spectrum shows this compound to be a mixture of epimers in the ratio 1 : 2.

Acidic Hydrolysis of the Diphenyl Derivative (14).—The diphenyl derivative (14) (100 mg) in acetic acid (10 ml) and concentrated hydrochloric acid (5 ml) was boiled under reflux for 4·0 h. The solution was cooled and evaporated to dryness under reduced pressure; the residue was extracted with ether and the acid fraction isolated in the usual way to give 1,3-*dihydro*-3,3-*diphenylnaphtho*[c]*furan*-1-*carboxylic acid* (15) (50 mg, 57%), m.p. 232—237° (from benzene–petroleum) (Found: C, 81·95; H, 5·15. $C_{25}H_{18}O_3$ requires C, 82·0; H, 4·9%), $\nu_{max.}$ 3200—2400, 1730, 1710, 1610, 1245, 1095, 880, 770, and 710 cm^{-1}, τ 1·7—2·7 (16H, m), 4·04 (1H, d, *J* 2 Hz), and 4·4—4·8 (1H, s, CO_2H, exch. D_2O), *m/e* 366 (*M*), 348, and 321 (3, 2·5, and 100%).

Oxidation of the Acid (7; R = H) *to* 2,3-*Dibenzoylnaphthalene*.—The keto-acid (7; R = H) (50 mg, 0·137 mmol) was added to chromium trioxide (48 mg, 0·48 mmol) in purified pyridine (5 ml) and the solution was stirred at 20° for 8 days, with the further addition (2 days, 4 days) of chromium trioxide (2 × 45 mg). Dilute hydrochloric acid (25 ml) was added to the solution, and the mixture was extracted with chloroform; the extract was washed with water, dried (Na_2SO_4), and evaporated. The crude product was chromatographed on silica (30 g) to give 2,3-dibenzoylnaphthalene [3] (11 mg, 0·0328 mmol), needles from benzene–petroleum, m.p. 127—129° (Found: C, 85·70; H, 5·0. Calc. for $C_{24}H_{16}O_2$: C, 85·75; H, 4·8%), $\nu_{max.}$ 1668 and 1647 cm^{-1}, $\lambda_{max.}$ 215, 259, 315, and 343 nm (ε 51,200, 51,200, 2260, and 3580), *m/e* 336 (*M*), 259, 243, 231, and 202 (35, 100, 2·5, 13, 3·6, and 50%).

An authentic * sample crystallised as rosettes from benzene–petroleum, m.p. 146·5—148°, $\nu_{max.}$ 1670 and 1655 cm^{-1}, *m/e* 336 (*M*), 259, 231, and 202 (37, 100, 15, and 50%).

Seeding of a concentrated solution of 2,3-dibenzoylnaphthalene obtained by oxidation, with a crystal of authentic material yielded rosettes, m.p. 146—148°.

Dehydration of the Acid (7; R = H) *and Diels–Alder Reactions of the Generated* 1,4-*Diphenylnaphtho*[2,3-c]*pyran*-3-*one* (5).—(A) *In the presence of* N-*phenylmaleimide*. The acid (100 mg, 0·273 mmol) and *N*-phenylmaleimide (49 mg, 0·28 mmol) in acetic anhydride (15 ml) were boiled under reflux under nitrogen for 1·25 h; an initial blue-green colour had disappeared after 0·5 h. The mixture was evaporated to dryness under high vacuum and the crude product chromatographed on silica (30 g); elution with benzene–ether (7 : 3) gave the adducts (17) and (18) (109 mg, 73%). Crystallisation from chloroform–ethanol gave the endo-*adduct* (17) (72 mg, 48%), m.p. 287—292° (Found: C, 80·1; H, 4·35; N, 2·9. $C_{32}H_{23}NO_4$ requires C, 80·6; H, 4·4; N, 2·7%), $\nu_{max.}$ 1755, 1710, 1600, 1190, 1000, 760, 750, and 700 cm^{-1}; owing to the insolubility of the compound, the n.m.r. spectrum of the *endo*-isomer was deduced by comparison of the spectrum of the crude adduct mixture with that of the pure *exo*-isomer: τ 1·7—3·3 (19H, m, aromatic), 3·8—4·2 (2H, m, aromatic), and 5·5br (2H, s, methine), *m/e* 477 ($M - CO_2$), 475, 430, and 330 (22, 10, 4, and 100%).

The mother liquor obtained after the removal of the *endo*-isomer gave the exo-*adduct* (18) (36 mg, 24%), m.p. 284—302° (decomp.) (from chloroform–methanol) (Found: C, 80·6; H, 4·55; N, 2·6%), $\nu_{max.}$ 1770, 1750, 1715, 1600, 1210, 745, and 695 cm^{-1}, τ 1·9—2·85 (19H, m, aromatic), 3·15br (1H, s, aromatic), 3·22 (1H, s, aromatic), 5·67 (1H, d, *J* 9 Hz), and 5·97 (1H, d, *J* 9 Hz), *m/e* 477 ($M - CO_2$), 475, 430, and 330 (36, 7, 2, and 100%).

(B) *In the presence of dimethyl fumarate*. The acid (100 mg, 0·273 mmol) and dimethyl fumarate (40 mg, 0·273 mmol) were dissolved in acetic anhydride (2·5 ml) and boiled under reflux under nitrogen for 2·5 h; an initial deep blue colour had disappeared after 1·2 h. The mixture was evaporated to dryness under high vacuum and the crude product chromatographed on silica (30 g). Elution with benzene–ether (9 : 1) gave the *ring*-c *adduct* (20) (50 mg, 35%), m.p. 222—225° (from chloroform–methanol) (Found: C, 75·2; H, 5·0. $C_{31}H_{24}O_6$ requires C, 75·6; H, 4·9%), $\nu_{max.}$ 1766, 1743, 1210, 1160, 995, and 755 cm^{-1}, τ 2·05—2·80 (15H, m, aromatic), 3·05 (1H, s, aromatic), 6·14 (1H, s, methine), 6·16 (1H, s, methine), 6·37 (3H, s), and 6·39 (3H, s), τ (C_6H_6) 5·9 (2H, s, methine), 6·85 (3H, s), and 6·86 (3H, s), *m/e* 492 (*M*), 348, 320, 291, 289, and 243 (10, 17, 100, 14, 13, and 11%).

Also obtained was a mixture of isomers of an alleged ring-B adduct (23), which could neither be separated nor crystallised (38 mg, 26%), τ 2·25—2·85 (14H, m, aromatic), 5·16 (1H, m, H-5), 5·32 (1H, s, H-10), 6·22—6·9 (2H, m, methine), and 6·43, 6·47, and 6·53 (6H, s, s, s), τ (C_6H_6) 4·95—5·32 (2H, m, methine H-5, H-10), 6·0—6·3 (1H, m, methine), 6·36—6·67 (1H, m, methine), 6·84 and 6·95 (3H, s, s), and 6·83 and 7·0 (3H, s, s), *m/e* 492 (*M*), 460, 448, 432, 416, and 388 (0·3, 6, 4, 2·5, 8, and 100%), $\nu_{max.}$ 1738, 1728, 1713, 1600, 1580, 1570, 1200, and 700 cm^{-1} (Found: *M*, 492·1586. $C_{31}H_{24}O_8$ requires *M*, 492·1573).

(C) *In the presence of dimethyl maleate*. The acid (120 mg, 0·328 mmol), and dimethyl maleate (2·5 g, 0·0174 mmol) in acetic anhydride (5·0 ml) were boiled under reflux under nitrogen for 1·25 h; an initial blue-green colour had disappeared after 1·0 h. The mixture was evaporated to dryness under high vacuum and the crude product was chromatographed on silica (30 g). Elution with benzene–ether (16 : 1) gave the endo-*adduct* (21) (20 mg, 12·5%), m.p. 252—256° (from chloroform–methanol) (Found: C, 75·7; H, 4·9. $C_{31}H_{24}O_6$ requires C, 75·6; H, 4·9%), $\nu_{max.}$ 1765, 1750, 1730, and 1210 cm^{-1}, τ 2·06—2·89 (16H, m,

* Conveniently prepared from 2-benzopyran-3-one generated by acetic anhydride dehydration of *o*-formylphenylacetic acid.[16]

aromatic), 5·81 (2H, s, methine), 6·48 (3H, s), and 6·54 (3H, s), *m/e* 492 (*M*), 448 (*M* − CO_2), 415, 388, and 357 (3·5, 100, 19, 72, and 15%). [Inspection of the crude column fraction that contained (21) prior to crystallisation indicated the presence of the dimethyl fumarate adduct (20); the identity was proven by examination of the n.m.r. spectra of solutions in deuteriochloroform and benzene. Further, the integral enabled the quantity of (20) (12 mg, 7·5%) to be calculated, although attempted isolation by crystallisation was not successful.]

Continued elution gave a mixture of two compounds which were separated on neutral alumina (Woelm, grade III). Elution with benzene gave the exo-*adduct* (22) (35 mg, 22%), m.p. 252—295° (from chloroform–methanol) (Found: C, 75·3; H, 4·8%), $\nu_{max.}$ 1771, 1756, 1220, 1165, 750, and 700 cm^{-1}, τ 2·1—2·7 (14H, m, aromatic), 2·83 (1H, s, aromatic), 3·09 (1H, s, aromatic), 5·83 (1H, d, *J* 11 Hz), 6·05 (1H, d, *J* 11 Hz), 6·45 (3H, s), and 6·60 (3H, s), *m/e* 448 (*M* − CO_2), 416, 388, and 357 (41, 3·5, 75, and 100%).

Continued elution gave a mixture of isomers of an alleged ring-B adduct (23), which could not be separated or crystallised (21 mg, 13%), τ 2·2—2·9 (14H, m, aromatic), 5·1—5·6 (2H, dd, H-5, H-10), 6·3—6·8 (2H, m, methine), and 6·4 and 6·65 (6H, s, s), *m/e* 492 (*M*), 480, 461, 433, and 388 (100, 12, 10, 4, and 7·5%) (Found: *M*, 492·1597).

The dimethyl maleate used in this experiment contained a small amount (<0·5% by g.l.c.) of dimethyl fumarate. The experiment was repeated with dimethyl maleate that had been freed from dimethyl fumarate by preparative g.l.c. (3-Benzoyl-2-naphthyl)phenylacetic acid (50 mg) and dimethyl maleate (400 mg) in acetic anhydride (3 ml) were boiled under reflux for 1·5 h. The n.m.r. spectrum of the crude product indicated adduct (22) (41%), adduct (21) (17%), and adduct (23) (35%) as the only products.

1,4-*Diphenylbenz*[g]*isoquinolin*-3-*ol* (6; R = H).—The methyl ester (7; R = Me) (100 mg, 0·263 mmol) and methanol (35 ml) in a Dewar vessel were mixed with liquid ammonia (40 ml) and kept under nitrogen for 14 days, during which time the solution turned deep red. The solution was evaporated to dryness and the residue chromatographed on silica (30 g); elution with benzene–ether (9 : 1) gave 1,4-*diphenylbenz*[g]*isoquinolin*-3-*ol* (6; R = H) (28 mg, 30%), m.p. 240—244° (from benzene–petroleum) (Found: C, 86·6; H, 5·0; N, 4·1. $C_{25}H_{17}NO$ requires C, 86·4; H, 4·9; N, 4·0%), $\nu_{max.}$ 2800—2300, 1595, 1530, 740, and 700 cm^{-1}, $\lambda_{max.}$ 260, 335, 352, and 433 nm (ε 67,900, 2840, 1760, and 6690), τ (90 MHz), 1·36 (1H, s, aromatic), 1·86 (1H, s, aromatic), and 2·05—2·77 (14H, m, aromatic), *m/e* 347 (*M*), 318, 240, and 215 (85, 100, 7, and 17%), *m** 291·43 (347 ⟶ 318).

Reaction of 1,4-*Diphenylbenz*[g]*isoquinolin*-3-*ol with Diazomethane*.—1,4-Diphenylbenz[g]isoquinolin-3-ol (6; R = H) (9·0 mg) in ethanol (1·0 ml), ether (10 ml), and benzene (2·0 ml) was treated at 0° with an excess of ethereal diazomethane for 4·0 h in the dark. Evaporation of solvents at 20° under high vacuum gave a yellow gum which was subjected to layer chromatography on silica. Development with benzene–ether (9 : 1) gave 3-*methoxy*-1,4-*diphenylbenz*[g]*isoquinoline* (6; R = Me) (4·5 mg, 48%), m.p. 191—192°, yellow needles from chloroform–methanol (Found: C, 86·3; H, 5·3; N, 4·1. $C_{26}H_{19}NO$ requires C, 86·4; H, 5·3; N, 3·9%), $\lambda_{max.}$ 262, 332, 355, and 434 nm (ε 65,030, 2360, 1545, and 7160), τ (90 MHz), 2·21—3·10 (16H, m, aromatic) and 6·08 (3H, s), *m/e* 361 (*M*), 336, 288, 259, and 202 (58, 33, 32, 100, and 67%). Extraction of a purple band from the thick layer plate gave 2-*methyl*-1,4-*diphenylmethylbenz*[g]*isoquinolin*-3-*one* (8; R = Me) (0·9 mg, 10%), a deep blue gum, *m/e* 361 (*M*), 333, 318, 302, 289, and 240 (49, 100, 29, 6, 4, and 41%) (Found: *M*, 361·1446. $C_{26}H_{19}NO$ requires *M*, 361·1467), $\lambda_{max.}$ ($CHCl_3$) 276, 542, 583, and 626sh nm, $\lambda_{max.}$ (cyclohexane) 275, 528sh, 576sh, 615, and 665 nm, $\lambda_{max.}$ (EtOH) 272 and 558 nm (ε 57,050 and 4755), $\nu_{max.}$ 1635, 1610, 1320, 1105, 870, 735, and 695 cm^{-1}, τ 2·1—3·15 (16H, m) and 6·27 (3H, s, NMe). The ready reaction of this compound with oxygen precluded purification for analysis.

Reaction of the Methyl Ester (7; R = Me) *with Methylamine*.—The methyl ester (114 mg) and methylamine (15 ml) were kept in a sealed tube at 20° under nitrogen for 30 days. The product was evaporated to dryness and treated with glacial acetic acid (5 ml); gentle warming on a water-bath for 10 min gave a deep blue solution. The solution was evaporated to dryness under high vacuum and the residue chromatographed on silica (20 g); elution with benzene–ethanol (9 : 1) afforded 2-methyl-1,4-diphenylbenz[g]isoquinolin-3-one (8; R = Me) (90 mg, 83%) as deep blue crystals, m.p. 195—200° (decomp.), on evaporation of the eluate under nitrogen. This material was shown by t.l.c. in several solvent systems to be identical with that prepared previously.

[2/1368 *Received*, 14*th June*, 1972]