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SUBSTITUTION AND ADDITION REACTIONS OF ISOINDOLES

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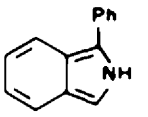
Abstract—1-Phenylisoindole reacts with toluene-*p*-diazonium chloride to give the azo derivative formed by electrophilic substitution at the free α position. However, attempted nitrosation of 1-phenylisoindole gave the product (3) of oxidative dimerisation, while the Mannich reaction gave 5,5'-diphenyldibenzopyrromethene. New routes to the latter system are described.

The dehydrogenation of isoindolines substituted at N-2 with electron withdrawing groups (CO_2Et, SO_2Tol-*p*) gives the corresponding isoindoles, which can be trapped with appropriate dienophiles to give a series of 4,9-epiminobenz[*f*]isoindoline derivatives.

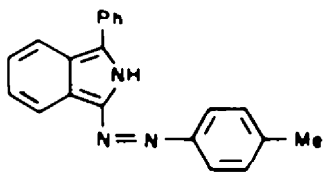
The isoindole system is a particularly reactive one, which shows three major reactions: polymerisation, the nature of which is not yet understood; diene reactivity across the C(1)–C(3) system; and electrophilic substitution at C(1)/C(3).[1] We describe here some experiments which seek to study reactions with less reactive electrophiles in which polymerisation (dimerisation) processes are encountered, and other experiments in which the diene reactivity is used to trap particularly destabilised isoindoles formed by the dehydrogenation of isoindolines.

Electrophilic substitution. The reagents used here were deliberately chosen to be mild ones: aryldiazonium ion, nitrous acid, and the Mannich reagent.

Reaction of 1-phenylisoindole (1) with diazotised *p*-toluidine in the normal way proceeded to give the azo derivative (2) in 63% yield. This appears to be the first such preparation of an azo dye based on the isoindole nucleus.



(1)



(2)

In neutral solvents compound (2) was orange (λ_{max} 467 nm), becoming purple (λ_{max} 547 nm) on acidification. The ready formation of (2) testifies the ease of electrophilic substitution in the isoindole nucleus.

However, attempts to carry out the other two electrophilic substitution reactions under mild conditions did not proceed in a straightforward way. Thus attempted nitrosation using sodium nitrite and acetic acid under argon was accompanied by colour changes which suggested the formation of intermediates; the isolated product was the tetradehydrodimer (3). This is the known product of autoxidation[2] of 1-phenylisoindole; presumably it arises here as shown in Scheme 1.

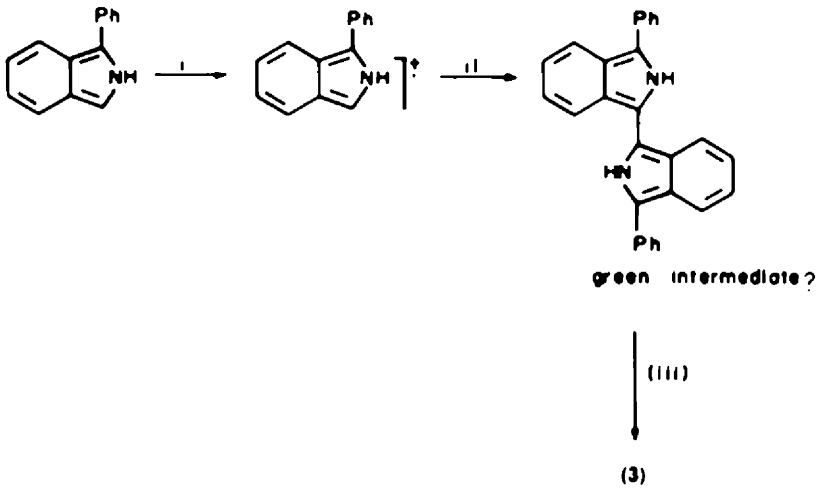
Attempted Mannich reactions under a variety of conditions gave no identifiable Mannich derivative; instead mixtures of the yellow tetradehydro dimer (3) and the blue dibenzopyrromethene (4) were obtained. The tetradehydro dimer (3) was usually a by-product; it may arise as in Scheme 1 by adventitious autoxidation, or by one electron transfer to the iminium cation. The dibenzopyrromethene presumably arises via the dipyrrylmethane condensation of the Mannich derivative, as shown in Scheme 2.

The blue dibenzopyrromethene (4) has been prepared (sometimes inadvertently) by several groups starting from isoindoles or their precursors.[1,3,4] The yields reported are low (1.5–13%), and we find that an extension of pyrrole chemistry to the isoindole series provides a much more satisfactory approach. Thus condensation of 1-phenylisoindole with 1-(*N,N*-dimethylaminomethylidene)-3-phenylisoindolenine (5) under acid conditions gave 44% of the dibenzopyrromethene (4). In another approach, 1-phenylisoindole was condensed with 1-formyl-3-phenylisoindole under acidic conditions to give 63% of (4).

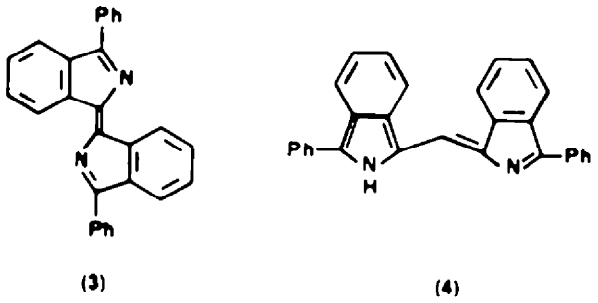
The dibenzopyrromethene (4) is royal blue in neutral solvents (λ_{max} 588 nm in chloroform); on acidification the solution becomes turquoise, and the low energy band shows a bathochromic shift (λ_{max} 625.5 nm) with a *ca* three fold intensification. The neutral solution fades in daylight due to photooxidation;[3] the protonated species is much more resistant in this respect.

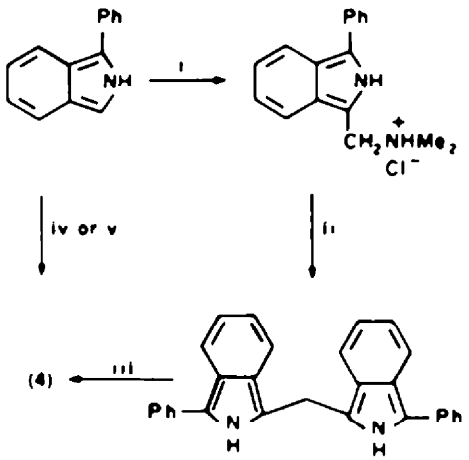
Diene reactivity. Isoindoles readily add dienophiles across the 1,3-positions to give the endo-adducts under mild conditions,[1] a reaction exemplified here by the addition of *N*-methylmaleimide to 2-benzylisoindole to give (6).

The dehydrogenation with quinones of isoindolines possessing electron withdrawing substituents (CO_2Me) at the 1- and 1,3-positions gives isoindoles which are relatively robust.[5] This type of reaction also proceeds with isoindolines possessing electron withdrawing sub-

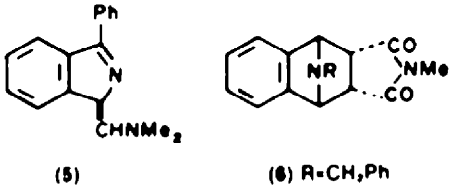


Scheme 1 (i) $H_2NO_2^{\cdot}$, $-e$ (ii) 1-phenylisoindole, $-2H^{+}$, $-e$ or 2x, $-2H^{+}$ (iii) air, $-2H$





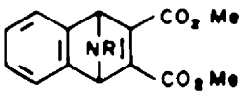
Scheme 2 (i) e.g. $CH_2{=}\dot{N}Me\text{-}Cl^{-}$, CH_2CN (ii) 1, H^{+}, or self condensation (iii) $-2H$ (air) (iv) 5, H^{+}, 44% (v) 1-formyl-1-phenylisoindole, H^{+}, 63% (yields not optimised)



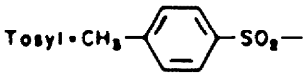
stituents (CO_2R, tosyl) at N2: although the corresponding isoindoles cannot be conveniently isolated, they can be trapped[9] with dienophiles

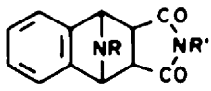
Thus when 2-carboethoxyisoindoline was kept with chloranil and dimethyl acetylenedicarboxylate in diglyme (145–150°, 27 h, N_2) the adduct (7) was obtained, although in low yield. Analogously, reaction with *N*-phenylmaleimide and DDQ in refluxing benzene gave the endo-adduct (8, 33%). The corresponding exo-adduct (9) was obtained by carrying out the dehydrogenation-trapping reaction in diglyme at 145° (30%), or by subjecting the endo-adduct (8) to these conditions (13%). The corresponding endo and exo adducts (10, 11) with *N*-methylmaleimide were obtained in an analogous manner. The assignment of stereochemistry was made throughout on the basis of coupling constants between the tertiary hydrogen atoms at the C-3a(C-9a) and C-4(C-9) positions of the 1,3-dioxobenz(f)isoindoline system (endo, $J \sim 3$ Hz, exo, $J \sim 0$ Hz). Dienophile exchange was observed. Treatment of the endo-adduct (10) with *N*-phenylmaleimide in diglyme at 145° gave a mixture of the *exo*-adducts (9, 23%) and (11, 19%).

2-Tosylisoindoline was also successfully dehydrogenated and trapped with DDQ in refluxing benzene to give the endo-adducts (12) and (13) in about 65% yield in each example. In this series equilibration with the exo isomer could be established only with difficulty presumably because of the greater steric demand of the tosyl group. Thus it was not successfully accomplished with the endo isomer (12) in xylene under reflux or in diglyme



(7) R = CO_2Et





(8) R = CO_2Et, R' = Ph, endo
(9) R = CO_2Et, R' = Ph, exo
(10) R = CO_2Et, R' = Me, endo
(11) R = CO_2Et, R' = Me, exo
(12) R = Tosyl, R' = Ph, endo
(13) R = Tosyl, R' = Me, endo
(14) R = Tosyl, R' = Ph, exo

at 145°; however, heating in carbitol at 185° gave a low yield (8%) of the exo-isomer (14).

Structures (such as 15) with a reduced imide ring were of interest since these are analogues of known analgetics.[9] Selective reduction of the imide carbonyl groups of (8), (12) and (13), was achieved with diborane to give the tertiary bases (15), (16) and (17), respectively in satisfactory yields. None of the compounds (15)–(17) exhibited sufficient biological activity in the primary screens to warrant further evaluation.

(15) R = CO_2Et, R' = Ph, endo
(16) R = Tosyl, R' = Ph, endo
(17) R = Tosyl, R' = Me, endo

EXPERIMENTAL

1-(p-Methylphenylazo)-3-phenylisoindole (2). *p*-Toluidine (0·122 g) was diazotised in the normal way [conc HCl (0·5 ml), water (2 ml), aq $NaNO_2$ (0·100 g in 0·2 ml), 0°] 1-Phenylisoindole (0·170 g)[10] in ethanol (1·5 ml) was added to the stirred solution under argon. A dark purple precipitate formed at once. The precipitate was removed by filtration and dissolved in ether (45 ml), the solution being washed with dilute hydrochloric acid (15 ml), then with aqueous sodium hydroxide (2 × 20 ml, solution goes orange), and finally with water. The ethereal solution was dried (Na_2SO_4) and taken to dryness, the oily orange residue being crystallised from ethanol–water to give dark orange needles (0·172 g, 63%) of 1-(p-methylphenylazo)-3-phenylisoindole, m.p. 118·5° (Found: C, 80·75; H, 5·65; N, 13·75%; M^+ = 311·143. $C_{21}H_{17}N_3$ requires C, 81·0; H, 5·5; N, 13·5%; M = 311·142). λ_{max}(EtOH) 247 (ε, 20 300), 254 (ε, 22 000), 261 (22 200), 274 (ε, 18 200), 283 (18 100), and 467 nm (37 200). λ_{max}(EtOH + conc HCl) 243 (15 000), 249 (ε, 14 600), 270 (18 400), 276 (ε, 17 000), 303 (ε, 12 900), 324 (16 100), and 547 nm (35 900). ν(Nujol) 3310, 1602, 1575, 1520, 1255, 1055, 820, and 760 cm^{-1}. δ[$(CD_3)_2CO$] 11·54 (bs, NH, observed at −53°), 8·37–7·12 (complex m, ArH), 2·82 (bs, H_2O impurity), and 2·32 (s, ArMe). *m/e* (152°) 311 (100, M), 310 (13), 283 (10), 193 (12), 192 (20), 165 (43), 106 (12) and 104 (17).

Attempted nitrosation/nitration. 1-Phenylisoindole (0·150 g), ether (6 ml), sodium nitrite (0·106 g), water (1·5 ml) and acetic acid (0·13 ml) were shaken together for 3 h at room temperature under argon (colour changes brown → green → yellow). Water (3 ml) was added, followed by aqueous sodium hydrogencarbonate until effervescence ceased. The ether layer was separated, the aqueous layer was extracted with ether (2 × 15 ml) and the organic solutions were combined, dried (Na_2SO_4) and taken to dryness. The residue was crystallised from ethanol–ethyl acetate to give yellowish orange needles (179 mg, 53%) of bis(1-phenylisoindolen-3-ylidene), 3, m.p. 258–259°, lit[7] m.p. 261–262° mixed m.p. 257–260°. λ_{max}(EtOH) 447 nm. λ_{max} (EtOH + HCl) 463 nm. *m/e* (167°) 382 (M, 100), 381 (18).

The reaction was repeated, but allowed to proceed for only 15 min. After neutralisation (aq $NaHCO_3$) the dark green product was submitted to preparative TLC (silica gel, petroleum–ether = 1:1) to furnish bis(1-phenylisoindolen-3-ylidene) (43%). The presence of a nitro or nitroso derivative could not be convincingly demonstrated.

5,5'-Diphenyldibenzopyrromethene (4). This substance is photosensitive: experiments were conducted in subdued light.

(i) *From 1-(N,N-dimethylaminomethylidene)-3-phenylisoindolenine and 1-phenylisoindole.* 1-(N,N-Dimethylaminomethylidene)-3-phenylisoindolenine (25 mg),[7] 1-phenylisoindole (21 mg), and 2M-hydrochloric acid (0·3 ml) were stirred for 18 h (argon, dark, room temperature). The mixture was basified (aq NaOH) and concentrated extraction with dichloromethane (3 × 30 ml), followed by drying the organic extract (Na_2SO_4) and removing the solvent gave a blue green residue which was purified by preparative TLC (silica gel, ether–petroleum = 1:1) to give a deep blue product (R_f 0·58) which was extracted with ether, and the ether removed to give a purple black residue (17·4 mg, 44%) of 5,5'-diphenyldibenzopyrromethene (4) m.p. 237–239° (lit[7] m.p. 240–241°). λ_{max}($CHCl_3$) 289 (23 800), 304 (ε, 22 300), 338 (ε, 15 100), 390 (ε, 3 900), and 588 nm (39 800). λ_{max}($CHCl_3$ + HCl) 298 (29 500), 335 (14 100), 350 (13 900), 580 (ε, 24 500), and 625·5 nm (108 000). *m/e* (226°) 396·164 (M, 100. $C_{30}H_{20}N_2$ requires 396·163), 233 (11), 198 (15), 197 (11), 193 (22), 165 (26), and 107 (15).

(ii) *From 1-formyl-3-phenylisoindole and 1-phenylisoindole.* Conc hydrochloric acid (3 drops) was added to a solution of 1-formyl-3-phenylisoindole (0·63 mg) and 1-phenylisoindole (1·07 mg) in tetrahydrofuran (1·5 ml). The mixture immediately became blue. After 3·5 h the solution was diluted with chloroform (15 ml), and extracted with brine (10 ml). The aqueous layer was back-extracted with chloroform, and the combined organic extracts were dried (Na_2SO_4) and the yield of the diphenyldibenzopyrromethene was estimated spectroscopically (63%). TLC and mixed TLC with the product above revealed only one component, (silica gel, petroleum–ethyl acetate = 1:2; silica gel, ether–petroleum = 1:1).

(iii) *From 1-phenylisoindole and formaldehyde.* Paraformaldehyde (0·33 mg) was dissolved in warm ethanol (1 ml) containing a trace of potassium hydroxide and added to 1-phenylisoindole (1·1 mg) in ethanol (1 ml) followed by conc HCl (3 drops). On addition of the acid, the mixture immediately became blue-green; it was shaken in air in the dark for 23 h. The pigment was purified and estimated spectroscopically as above (15% yield).

(iv) *Attempted Mannich reaction.* Attempts to carry out the Mannich reaction on 1-phenylisoindole under a variety of conditions gave a mixture of the yellow oxidative dimer (3) and the blue dibenzopyrromethene (4). These products could be readily separated and identified by TLC (silica gel, benzene–cyclohexane = 3:1, 4, R_f 0·54; 3, R_f 0·32). Thus with dimethylamine and paraformaldehyde in ethanol (argon, dark, 4 h) 4 (20%) and 3 (25%) were obtained. With *N,N*-dimethylmethylidene ammonium chloride in acetonitrile (3 h, nitrogen, dark) the dibenzopyrromethene was the major product.

2-Carbomethoxyisoindoline. Methyl carbamate (0·25 g) in anhydrous dimethylformamide (3 ml) was added dropwise to a stirred mixture of sodium hydride (0·33 g) and *o*-xylene dibromide (1·0 g) in anhydrous dimethylformamide (5 ml) under

nitrogen. The mixture was stirred at room temperature for 2 h, and then poured into ice water (50 ml). The resulting precipitate was removed by filtration and crystallised (charcoal) from methanol–water to give glistening white plates (0.31 g, 52%) 2-carbomethoxyisoindoline, m.p. 108.5–109° (lit[11] m.p. 109–109.5°).

2-Carboethoxyisoindoline was prepared analogously (49%), m.p. 87–88° (lit[11] m.p. 87°), as was 2-carbobenzyloxyisoindoline (28%), m.p. 104–106°. Found: C, 75.75; H, 5.8; N, 5.7. $C_{16}H_{15}NO_2$ requires C, 75.85; H, 5.95; N, 5.55%.

endo - 4,9 - *Benzylepimino* - 3a,9a - *dihydro* - 2 - *methyl* - 1,3 - *dioxobenz*[*f*] - *isoindoline* (6). *N*-Methylmaleimide (0.329 g) in tetrahydrofuran (3 ml) was added to a solution of 2-benzylisoindole (0.42 g)[11] in tetrahydrofuran (2.5 ml) stirred under nitrogen. A cream coloured precipitate formed after about 10 min. After 4 h the solid was removed by filtration and crystallised from ethanol to give shiny white plates (0.404 g, 63%) of the endo-adduct (6), m.p. 159–160.5° (dec). Found: C, 75.3; H, 5.85; N, 8.7%. M^+ 318.1375. $C_{20}H_{18}N_2O_2$ requires C, 75.45; H, 5.7; N, 8.8%. *M* 318.137 (KBr) 1760, 1685, 1430, 1283, 1128, 763 and 740 cm^{-1} δ(CDCl$_3$) 7.35–7.0 (m, ArH), 4.54 (m, H at C4,C9), 3.65 (m, H at C3a,C9a), 3.35 (s, PhCH$_2$) and 2.24 (2, NMe). *m/e* (153°) 318(M, 16), 207 (53, M-imide), 111 (23, imide), and 91 (100, C$_7$H$_7^+$).

Dehydrogenation of 2-substituted isoindolines. Isolation of the resulting isoindoles as Diels–Alder adducts. Dimethyl - 1,4 - *carboethoxyepimino* - 1,4 - *dihydronaphthalene* - 2,3 - *dicarboxylate* (7). 2-Carboethoxyisoindoline (0.15 g), chloranil (0.26 g) and dimethyl acetylenedicarboxylate (0.58 g) were stirred in diglyme (6 ml) at 145–150° (27 h, N_2). The solvent and excess dienophile were removed *in vacuo*, aqueous sodium hydroxide (5%, 6 ml) was added, and the mixture was extracted with chloroform (2 × 15 ml). The chloroform solution was dried (Na_2SO_4), concentrated, and submitted to preparative TLC (silica gel, petroleum–ethyl acetate = 2:1). The component with R_f 0.34, dimethyl - 1,4 - carboethoxyepimino - 1,4 - dihydronaphthalene - 2,3 - dicarboxylate, was recovered as an oil (50 mg, 19%) (Found: M^+ = 331.105. $C_{19}H_{17}NO_4$ requires 331.106). ν_{max}(CCl$_4$) 1725, 1708, 1695, 1620, 1320, 1245, 1195, and 1090 cm^{-1}. δ(CDCl$_3$) 7.41 (m, H at C5,C8), 7.04 (m, H at C6,C7), 5.83 (s, H at C1,C4), 4.08 (q, *J* = 7 Hz, CH$_2$Me), 3.78 (s, OCH$_3$), and 1.21 (t, *J* = 7 Hz, CH$_2$Me). *m/e* (54°) 331 (M, 26), 232 (39), 213 (9), 211 (9), 200 (48), 190 (12), 189 (100, M-dienophile), 174 (10), 171 (86), 147 (11), 146 (83), 143 (31) and 142 (9, dienophile). (On prolonged storage at 0° the oil solidified and then had m.p. 73.5–75°.)

endo - 4,9 - *Carboethoxyepimino* - 3a,9a - *dihydro* - 1,3 - *dioxo* - 2 - *phenylbenz*[*f*] - *isoindoline* (8). 2 - Carboethoxyisoindoline (0.78 g), *N* - phenylmaleimide (2.20 g), 2,3 - dichloro - 5,6 - dicyanobenzoquinone (DDQ, 1.13 g), and benzene (85 ml) were refluxed with stirring (N_2, 8 h). Next morning the precipitated quinol was removed, and the filtrate was concentrated and treated with ether to precipitate excess *N*-phenylmaleimide. The filtrate was again concentrated, and subjected to column chromatography (silica gel, 20 × 2.5 cm, acetone–petroleum = 1:2) appropriate fractions being detected by TLC (same system, R_f 0.37) and combined. Removal of solvent, and crystallisation from ethanol gave white needles (0.49 g, 33%) of endo - 4,9 - carboethoxyepimino - 3a,9a - dihydro - 1,3 - dioxo - 2 - phenylbenz[*f*]isoindoline, m.p. 166–166.5°. Found: C, 69.75; H, 5.0; N, 7.65%. M^+ = 362.126. $C_{21}H_{18}N_2O_4$ requires C, 69.6; H, 5.0; N, 7.75%. *M* = 362.127. λ_{max}(EtOH) 256 (ε, 740), 263 (660), and 269.5 nm (400). ν_{max}(Nujol) 1780, 1715, 1600, 1500, 1338, 1270, 1235, 1195, 1180, 1145, 1085, 740 and 690 cm^{-1}. δ(CDCl$_3$) 7.50–7.14 (7H) and 6.41 (2H) (m, m, ArH), 5.63 (m, H at C4,C9), 4.14 (q, *J* = 7 Hz, CH$_2$Me), 3.88 (m, H at C3a,C9a), and 1.22 (t, *J* = 7 Hz, CH$_2$Me). *m/e* (161°) 362 (M, 9), 317 (14), 223 (23), 191 (29), 174 (27), 169 (11), 161 (65), 130 (63), 129 (65), 128 (63), 119 (42) and 115 (100).

exo - 4,9 - *Carboethoxyepimino* - 3a,9a - *dihydro* - 1,3 - *dioxo* - 2 - *phenylbenz*[*f*] - *isoindoline* (9). (a) *Directly, by dehydrogenation and cycloaddition at 145°.* 2-Carboethoxyisoindoline (0.23 g), *N*-phenylmaleimide (0.23 g), chloranil (0.32 g) and diglyme (9 ml) were stirred at 145° (N_2, 8 h). The solvent was removed *in vacuo* and ether (15 ml) was added to the residue, and the mixture kept overnight at 4°. The resulting solid was crystallised from ethanol to give white needles (0.13 g, 30%) of the exo-adduct (9), m.p. 185–186°. Three crystallisations from ethanol raised the m.p. to 186.5–187°. Found: C, 69.8; H, 5.1; N, 7.8%. λ_{max}(EtOH) 256 (ε, 1050), 263 (930) and 270.5 nm (580). ν_{max}(CHCl$_3$) 1775, 1710, 1600, 1505, 1390, 1325, 1190, 1095, 885, and 850 cm^{-1}. δ(CDCl$_3$) 7.51–7.09 (complex m, ArH), 5.61 (s, H at C4,C9), 3.97 (q, *J* = 7 Hz, –CH$_2$Me), 3.03 (s, H at C3a,C9a) and 1.12 (t, *J* = 7 Hz, –CH$_2$Me). *m/e* (99°) 362 (M, 1), 189 (100, M-dienophile), and 173 (9, dienophile). (b) *By isomerisation of the endo-adduct.* The endo-adduct (0.161 g), *N*-phenylmaleimide (0.016 g), and diglyme (3 ml) were heated at 145–150° for 19 h under nitrogen. The diglyme was removed *in vacuo* and the residue was submitted to preparative TLC (silica gel, petroleum–ethyl acetate = 1:1). The mixture consisted essentially of *N*-phenylmaleimide (R_f 0.51) and the exo-adduct (R_f 0.41). The latter fraction was crystallised from ethanol to give the exo-adduct (22 mg, 13%) identical (mixed m.p., TLC, NMR) with the previous sample. Mixed m.p. with endo-adduct 143.5–147°.

endo and exo - 4,9 - *Carboethoxyepimino* - 3a,9a - *dihydro* - 2 - *methyl* - 1,3 - *dioxobenz*[*f*]*isoindolines* (10, 11). In an analogous manner, reaction of 2-carboethoxyisoindoline, *N*-methylmaleimide and DDQ in benzene (28 h) gave in 26% yield endo - 4,9 - carboethoxyepimino - 3a,9a - dihydro - 2 - methyl - 1,3 - dioxobenz[*f*]isoindoline (10), white crystals, m.p. 140–141° from ethanol–ether (Found: C, 64.0; H, 5.55; N, 9.4%. M^+ = 300.111. $C_{16}H_{16}N_2O_4$ requires C, 64.0; H, 5.35; N, 9.35%. *M* = 300.111). δ(CDCl$_3$) 7.39–7.14 (m, ArH), 5.57 (m, H at C4,C9), 4.13(q), 3.72 (m, H at C3a,C9a), 2.31 (s, NMe), and 1.28 (t). Equilibration of this endo-adduct in diglyme at 145–150° for 18 h in the presence of a small proportion of the dienophile as before gave in 44% yield the corresponding exo-adduct (11), fine white needles, m.p. 164–164.5° from ethyl acetate–petroleum. Found: C, 63.65; H, 5.56; N, 9.4%. M^+ = 300.110. δ(CDCl$_3$) 7.50–7.15 (m, ArH), 5.50 (s, H at C4,C9), 3.98 (q), 3.03 (s, NMe), 2.90 (s, H at C3a,C9a) and 1.13 (t).

Dienophile exchange. endo - 3a,9a - Dihydro - 4,9 - carbethoxyepimino - 2 - methyl - 1,3 - dioxobenz[*f*]isoindoline (0.300 g), *N*-phenylmaleimide (0.220 g) and diglyme (4 ml) were heated at 145–150° (16 h, argon). The solvent was removed *in vacuo*, the residue in dichloromethane was washed with water, dried, and submitted to column chromatography (silica gel, 22.5 × 2.5 cm, ether–petroleum–dichloromethane = 4:2:1). Fractions of *ca* 5 ml were collected and were assessed by TLC in the usual way: fractions 15–19 gave 85 mg (23%) of the exo-*N*-phenyl adduct (9) identical (mixed m.p., NMR, IR) with the sample prepared earlier. Fractions 21–27 contained 78 mg of a mixture of the starting material and its exo isomer. This mixture was separated by preparative TLC (silica gel, ethyl acetate–petroleum = 1:1) to give the starting material (11 mg, less mobile) together with 58 mg (19%) of the exo isomer (more mobile), identical (m.p., NMR, IR) with the sample prepared in the experiment described immediately above.

endo- and exo - 3a,9a,*Dihydro* - 1,3 - *dioxo* - 2 - *phenyl* - 4,9 - (*toluene* - *p* - *sulphonyl*)*epiminobenz*[*f*]*isoindoline* (12, 14). 2(Toluene - *p* - sulphonyl)isoindoline[14] (0.69 g), DDQ (0.71 g), *N*-phenylmaleimide (0.89 g) and benzene (120 ml) were stirred under reflux (29 h, N_2) and then allowed to cool overnight. The hydroquinone was filtered off and the filtrate was concentrated to a brown oil, which was treated with ether. This caused the crude product to separate; it was removed, and the filtrate was again concentrated and treated with ether to obtain a further quantity. The combined solids were washed with ether, and then crystallised from ethanol (charcoal) to give fine white needles (0.72 g, 64%) of endo - 3a,9a - dihydro - 1,3 - dioxo - 2 - phenyl - 4,9 - (toluene - *p* - sulphonyl)epiminobenz[*f*]isoindoline (12), m.p. 220–221° (Found: C, 67.45; H, 4.5; N, 6.3; S, 6.9%. $C_{29}H_{20}N_2O_6S$ requires C, 67.55; H, 4.55; N, 6.3; S, 7.25%). ν_{max}(Nujol) 1780, 1720, 1595, 1495, 1380, 1340, 1160, 810, 740 and 690 cm^{-1}. δ(CDCl$_3$) 7.50 (d, part of AA'BB', ArH ortho to SO$_2$ substituent), 7.37–6.92 (m, including apparent s at 7.07, 9 ArH), 6.31 (m, ArH ortho to N substituent), 5.47 (m, H at C4,C9), 4.07 (m, H at C3a,C9a), and 2.30 (s, Me). *m/e* (221°) M^+ not detected, 272 (15), 221 (94, m-dienophile), 207 (16), 173 (53, dienophile), 155 (26), and 91 (100).

Attempts to isomerise this endo-adduct in xylene under reflux (9 h) and in diglyme at 145° (17 h) were unsuccessful. Equilibration in carbitol at 185–190° (21 h, N_2) in the presence of a small proportion of *N*-phenylmaleimide as before, led to much decomposition, but gave a low yield (8%) of a substance believed to be the isomeric exo-adduct (14) on the basis of its NMR spectrum. δ(CDCl₃) 7.69–6.95 (complex, m, 13 ArH), 5.46 (s, H at C4,C9), 3.08 (s, H at C3a,C9a) and 2.30 (s, Me).

endo - 3a,9a - Dihydro - 2 - methyl - 1,3 - dioxo - 4,9 - (toluene - p - sulphonyl)epiminobenz[f]isoindoline (13). 2 - (Toluene - *p* - sulphonyl)isoindoline (1.74 g), DDQ (1.60 g), *N*-methylmaleimide (0.80 g) and benzene (140 ml) were stirred under reflux (25 h, argon). The solvent was removed, dichloromethane (100 ml) was added, and the solution was extracted with aqueous sodium hydroxide (2M, 5 × 100 ml). The organic layer was dried and concentrated. The resulting brownish yellow solid was crystallised from ethanol (charcoal) to give glistening white plates (1.58 g, 65%) of endo - 3a,9a - dihydro - 2 - methyl - 1,3 - dioxo - 4,9 - (toluene - *p* - sulphonyl)epiminobenz[f]isoindoline (13) m.p. 229.5–230.5° (dec) (Found: C, 62.55; H, 4.7; N, 7.2; S, 8.25%; M^+ = 382.0985. $C_{20}H_{18}N_2O_4S$ requires C, 62.8; H, 4.75; N, 7.3; S, 8.4%; M = 382.099). ν_{max}(Nujol) 1780, 1705, 1600, 1348, 1167, 993, 830, 763, and 690 cm^{-1}. δ(CDCl₃) 7.90, 7.06 (AA'BB' of tosyl ArH), 7.00 (s, remaining ArH), 5.36 (m, H at C4,C9), 3.89 (m, H at C3a,C9a), 2.30 and 2.23 (s, s, CMe and NMe). *m/e* (20%) 382 (M, 2), 273 (42), 207 (36), and 155 (100).

Reduction of Diels–Alder adducts with diborane. The endo-adduct (8) (0.540 g) in anhydrous tetrahydrofuran (8 ml) was added dropwise to a stirred solution of diborane in tetrahydrofuran (1M, 6 ml) under nitrogen at 0°. The reaction was kept at 0° for 30 min, then stirred at room temperature for 4.5 h. Aqueous hydrochloric acid (2M, 4 ml) was added carefully, followed by water (15 ml), and the tetrahydrofuran was distilled off. The residue was made alkaline (aq. NaOH) and extracted with dichloromethane (4 × 50 ml). The extracts were dried (K_2CO_3) and evaporated to dryness. The residue was crystallised (charcoal) and recrystallised from methanol to give small white needles (0.26 g, 52%) of endo - 4,9 - carboethoxyepimino - 3a,9a - dihydro - 2 - phenylbenz[f]isoindoline (15), m.p. 147–148° (dec) (Found: C, 75.0; H, 6.6; N, 8.2%; M^+ = 334.169. $C_{21}H_{22}N_2O_2$ requires C, 75.4; H, 6.65; N, 8.4%; M = 334.168). λ_{max}(EtOH) 252 (15,200) and 298 nm (2,400). ν_{max}(Nujol) 1710, 1600, 1505, 1370, 1355, 1270, 1245, 1205, 1100, 750, and 692 cm^{-1}. δ(CHCl₃) 7.35–6.86 (m, 6 ArH), 6.46 (t, J = 6 Hz, H at C4 of Ph), 6.11 (m, H at C2,C6 of Ph), 5.14 (m, H at C4,C9), 4.10 (q), 3.31 (m, H at C3a,C9a), 3.03–2.56 (m, H at C1,C3) and 1.18 (t). *m/e* (92%) 334 (78, M), 190 (13), 189 (100, retro Diels–Alder), 146 (31), 120 (11), and 117 (29).

The following isoindolines were prepared in a similar way. endo - 3a,9a - Dihydro - 2 - phenyl - 4,9 - (toluene - *p* - sulphonyl)epiminobenz[f]isoindoline (16) from (12) in 83% yield. White needles, m.p. 223–224° (dec) from ethanol–chloroform (Found: C, 71.8; H, 5.75; N, 6.7; S, 7.5%; M^+ = 416.155. $C_{25}H_{20}N_2O_2S$ requires C, 72.1; H, 5.8; N, 6.75; S, 7.7%; M = 416.156). endo - 3a,9a - Dihydro - 2 - methyl - 4,9(toluene - *p* - sulphonyl)epiminobenz[f]isoindoline (17), from (13) in 60% yield. Fine white needles, m.p. 134.5–135° from ethanol–petroleum (Found: C, 67.3; H, 6.3; N, 7.25; S, 8.25%; M^+ = 354.140. $C_{20}H_{22}N_2O_2S$ requires C, 67.8; H, 6.3; N, 7.9; S, 9.05%; M = 354.140).

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