Synthesis and Reactions of 2,3-Dihydro-oxazolo[2,3-*a*]isoindol-5(9b*H*)-ones

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The synthesis and reactions with nucleophiles of 2,3-dihydro-oxazolo[2,3-*a*]isoindol-5(9b*H*)-ones are described.

Syntheses of 2,3-dihydro-oxazolo[2,3-*a*]isoindol-5(9b*H*)-ones have been reported only rarely in the literature,[1-4] and there appears to be no description of the chemistry of these compounds. We report here the synthesis of novel oxazolo[2,3-*a*]-isoindolones by the extension of a previously described route,[2,4] the first description of the parent molecule, and the reactions of these compounds with a variety of nucleophiles.

Results and Discussion

In the course of attempts to make substituted furans 2-furyl-lithium (**1a**) was treated with *N*-(2-bromoethyl)phthalimide (**2**). The only product obtained after chromatography was identified as 2,3-dihydro-9b-(2-furyl)oxazolo[2,3-*a*]isoindol-5(9b*H*)-one (**3a**). The ^{13}C and the highly complex ^{1}H n.m.r. spectral assignments were important in establishing the structure of this product, particularly, the ^{13}C n.m.r. signal (96.0 p.p.m.) attributable to a quaternary carbon atom (low intensity due to long relaxation time), and the observation of an unusually lowfield proton signal for $H_{B'}$ in (**3**), previously reported by Aeberli and Houlihan.[3] The latter may be ascribed to the deshielding influence of the adjacent carbonyl group. These features appear to be diagnostic of these molecules.

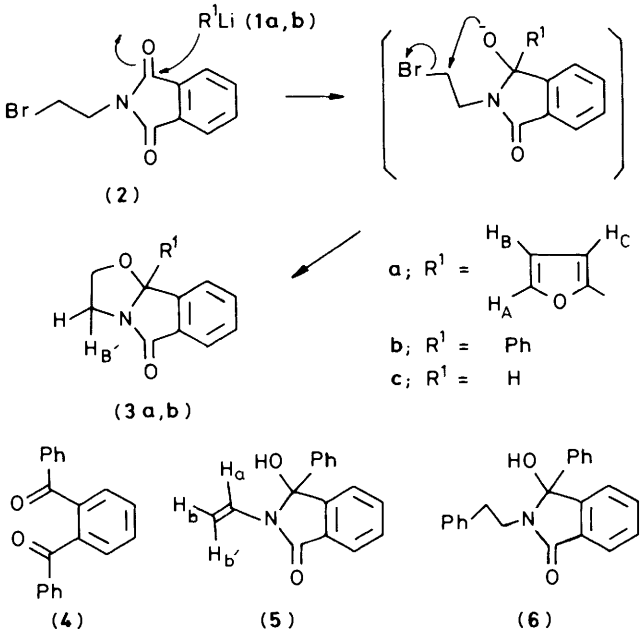
The formation of (**3a**) thus extends the observations that lithium ester enolates[4] and lithium phenylacetylide[2] react with (**2**) to give oxazolo[2,3-*a*]isoindolones.

The reaction was investigated in more detail using phenyl-lithium (**1b**) as the nucleophile. Slow addition of (**1b**) to (**2**) gave (**3b**) in 54% yield (method A), whereas the inverse addition (method B) gave a four-component mixture. These components were separated by chromatography and identified as (**3b**), *o*-dibenzoylbenzene (**4**), 3-phenyl-*N*-vinylphthalimidine (**5**), and *N*-phenethyl-3-phenylphthalimidine (**6**). These last three products are presumed to arise from the presence of an excess of (**1b**). The diketone (**4**) is formed from the reaction of the initial product (**3b**) with (**1b**) (*vide infra*), and the phthalimidines (**5**) and (**6**) may be produced by 'capture' of an uncyclised intermediate by reaction with a second molecule of (**1b**), acting in one instance as a base [to give (**5**)], and in the other as a nucleophile [to give (**6**)]. This explanation would imply that cyclisation is the rate-limiting step in the formation of (**3b**).

The parent molecule (**3c**) has not been described and is not available using the route illustrated above. It has now been prepared, in low yield, by the reduction of (**2**) with sodium borohydride[5] to the phthalimidine (**7**), which cyclises to give (**3c**) on treatment with potassium t-butoxide in t-butyl alcohol (Scheme 2). Subsequently, we have established that combination of these two steps without isolation of (**7**) has simplified this preparation and has improved the yield.

The presence of several electrophilic positions in the oxazolo-[2,3-*a*]isoindolone structure (**3**) suggested that the reactions of (**3**) with nucleophiles would be of some interest because of the variety of possible products.

The parent compound (**3c**) does not, in fact, react with strongly basic nucleophiles, presumably as a consequence of its

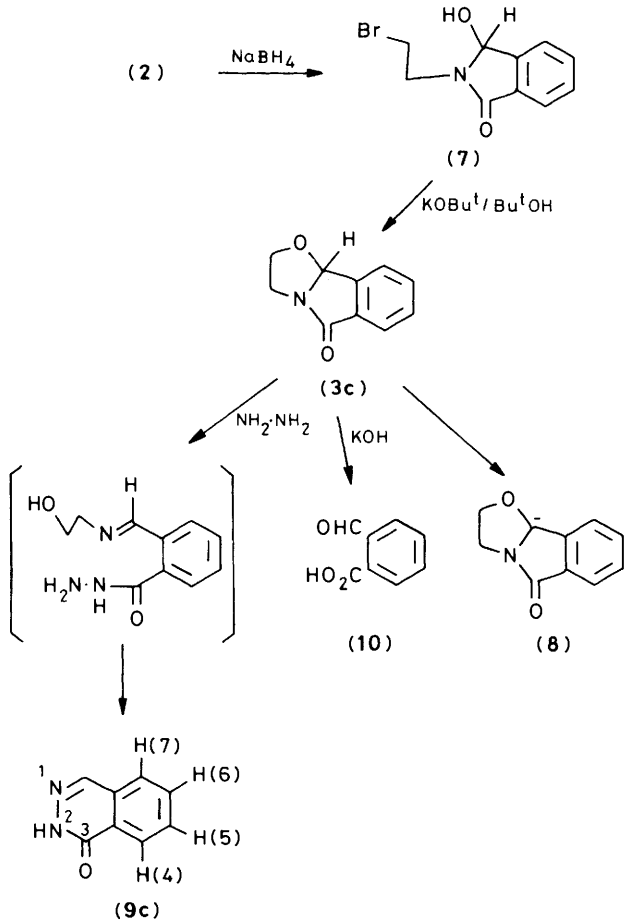


Scheme 1.

deprotonation to give the anion (**8**), which is not susceptible to nucleophilic attack. This is supported by strong base-catalysed exchange data from n.m.r. experiments. However (**3c**) does react with hydrazine and with aqueous sodium hydroxide, in both cases at the carbonyl group; with the former to give the oxophthalazine (**9c**), and with the latter to give *o*-formylbenzoic acid (**10**). Nucleophilic attack at the carbonyl group presumably results in the ring-opened intermediate imine depicted in Scheme 2 which can then fragment and cyclise to give (**9c**), whereas (**10**) is formed as a direct consequence of fragmentation. N.m.r. experiments have established that (**10**) is also formed by acid-catalysed hydrolysis of (**3c**).

Similar reactions of the 9b-substituted oxazolo[2,3-*a*]iso-indolones (**3a**) and (**3b**), with hydrazine gave the phthalazin-4-ones (**9a**) and (**9b**), and (**3b**) with aqueous base gave the oxo acid (**11**). In contrast to the inability of (**3c**) to react with strongly basic nucleophiles, (**3a**) and (**3b**) follow the path illustrated in Scheme 3.

Thus, the furyl compound (**3a**) with 1 equiv. of furyl-lithium (**1a**) gave *o*-di-2-furoylbenzene (**12**), in poor yield after aqueous work-up and subsequent chromatography. Similarly the phenyl compound (**3b**) gave (**4**) on reaction with phenyl-lithium and, more interestingly, gave the unsymmetrical diketone (**13**) in low yield on reaction with furyl-lithium (Scheme 3). The formation of (**13**) exemplifies the consecutive, selective functionalisation of the carbonyl groups of the symmetrical starting material (**2**). The diketones (**4**) and (**12**) were further characterised by their



Scheme 2.

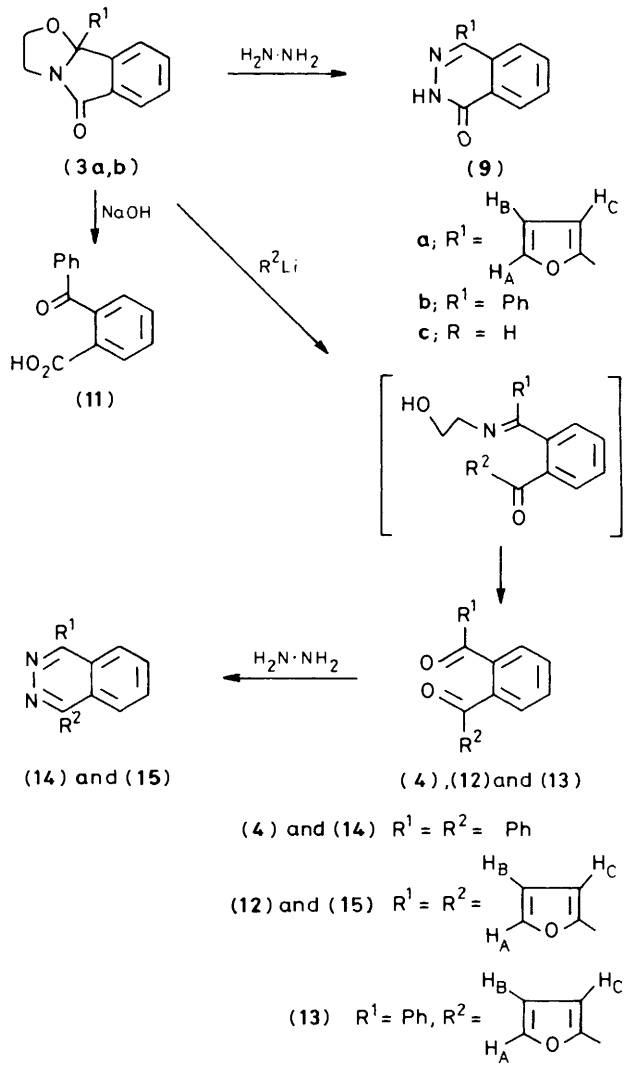
condensation with hydrazine which produced the corresponding phthalazines (**14**) and (**15**).

Even though some of these transformations proceed in low yield we feel that the products formed may have some synthetic utility. The use of *N*-(2-bromoethyl)phthalimides substituted in the aromatic ring would widen the scope of these reactions, although the question of regioselectivity has not been addressed in the present work. This scope would be limited only by the availability of the appropriately substituted phthalic acids.

Experimental

I.r. spectra were determined with a Perkin-Elmer 157G or 297 instrument for KBr discs, Nujol mulls, or liquid films. ^{1}H and ^{13}C N.m.r. spectra were recorded using a Perkin-Elmer R12B (60 MHz) or a Jeol JNM-PMX60 (60 MHz) spectrometer operating in the continuous-wave mode and a Bruker WP-80 (80 MHz), a Bruker HFX-90 (90 MHz) or a Bruker WM-360 (360 MHz) instrument operating in the Fourier-transform mode[tetramethylsilane or 2,2,3,3-tetradeuterio-3-(trimethylsilyl)propionic acid, sodium salt were used as internal standard]. Resonances are reported as p.p.m. downfield from tetramethylsilane position on the δ scale.

All products were routinely checked for homogeneity by t.l.c. on silica-gel plates (E. Merck, 60F254, 0.25 mm) using the solvents indicated in the text. The spots were located either by filtered u.v. light ($\lambda_{max.}$ 254 and 365 nm), or by iodine. Reaction times were not optimised. Light petroleum had b.p. 60—80 °C.



Scheme 3.

Preparation of 2,3-*Dihydro*-9b-(2-*furyl*)*oxazolo*[2,3-a]*isoindol*-5(9bH)-*one* (**3a**).—A solution of 2-furyl-lithium in tetrahydrofuran (THF) was prepared by adding n-butyl-lithium (1.55 M-solution in hexane; 65 ml, 0.1 mol) to a solution of furan (6.8 g, 0.1 mol) in dry THF (60 ml) under positive nitrogen pressure, and then warming the mixture at 40 °C for 3 h. The orange solution so obtained was cooled to −30 °C and a pre-cooled solution of *N*-(2-bromoethyl)phthalimide (25.4 g, 0.1 mol) in THF (70 ml) was added during 20 min. After completion of the addition the reaction mixture was stirred for 4 h without external cooling, and then worked up by addition of water (100 ml) and subsequent extraction with ethyl acetate and drying (Na_2SO_4) of the extracts. Filtration and evaporation afforded an oily residue (21.24 g). A portion of the oil (3.12 g) was chromatographed on a silica-gel column (ART 9385) with ethyl acetate–cyclohexane (1 : 2) as eluant to give a gum (0.79 g) which crystallised to a solid (0.40 g) after trituration with light petroleum at 0 °C. The bulk crude mixture was columned likewise. The two batches of solid product were combined and recrystallised from ethyl acetate–light petroleum to afford *product* (**3a**) (3.68 g, 15%), m.p. 55.5—58.5 °C (Found: C, 69.5; H, 4.5; N, 5.8. $C_{14}H_{11}NO_3$ requires C, 69.71; H, 4.56; N, 5.81%); $\nu_{max.}$ (KBr disc) 1 763, 1 705, 1 390, 1 064, and 720 cm^{-1}; δ_H($CDCl_3$) 3.46—3.58 (1 H, m) and 4.10—4.24 (1 H, m) [NCH_2],

4.24—4.36 (2 H, m, OCH_2), 6.34 (1 H, m, H_B), 6.46 (1 H, m, H_C), 7.46 (1 H, m, H_A), 7.50—7.72 (3 H, m), and 7.76—7.84 (1 H, m, Ph); $\delta_C(CDCl_3)$ 42.5 (NCH_2), 70.2 (OCH_2), 96.0 (quaternary C), 108.7 and 110.1 (furan C-3, C-4), 123.8, 124.4 and 130.5 (phenyl), 131.6 (phenyl quaternary), 133.2 (phenyl), 143.8 (furan C-5), 144.4 (quaternary phenyl), 150.6 (furan C-2), and 173.2 (carbonyl); M^+ 241 and fragmentation consistent with proposed structure.

Preparation of 2,3-*Dihydro*-9b-*phenyloxazolo*[2,3-a]*isoindol*-5(9bH)-*one* (**3b**).—*Method A.* To a solution of *N*-(2-bromoethyl)phthalimide (12.7 g, 0.05 mol) in dry THF (50 ml), stirred and cooled at −40 °C was added during 35 min under positive nitrogen pressure a pre-cooled solution of phenyl-lithium (1.9 M-solution in cyclohexane–diethyl ether 7:3; 26.3 ml, 0.05 mol) previously diluted with dry THF (50 ml). After completion of the addition the reaction mixture was stirred for 40 min at −40 °C and then brought to room temperature and stirred for 17 h. It was then worked up by careful addition of water (25 ml) and extraction with ethyl acetate (3 × 25 ml) followed by drying (Na_2SO_4) of the combined extracts, filtration, and evaporation to give a solid which was recrystallised from ethyl acetate–light petroleum to afford (**3b**) (6.83 g, 54%), m.p. 145—148 °C (lit.,[3] 147—149 °C) (Found: C, 76.3; H, 5.2; N, 5.6. Calc. for $C_{16}H_{13}NO_2$: C, 76.49; H, 5.18; N, 5.58%); $\nu_{max.}$ (KBr disc) 3 045, 2 975, 2 895, 1 718, 1 462, 1 347, 754, and 700 cm^{-1}; $\delta_H(CDCl_3)$ 3.07—3.40 (1 H, m, NC*H*H), 3.98—4.53 (3 H, m, NC*H*H + OCH_2), and 7.24—7.93 (9 H, m, ArH); $\delta_C(CDCl_3)$ 41.6 (NCH_2), 70.2 (OCH_2), 100.5 (O*C*(Ph)N), 123.6, 124.3, 125.8, 128.8 and 130.1 (Ar), 131.3 (quaternary phenyl), 133.2 (Ar), 138.3 and 147.3 (quaternary phenyl), and 173.9 (carbonyl); M^+ 251.00.

Method B. To phenyl-lithium (1.9 M-solution in cyclohexane–diethyl ether 7:3; 53 ml, 0.1 mol) diluted with dry THF (70 ml), stirred and cooled at −40 °C was added during 40 min under positive nitrogen pressure a pre-cooled solution of *N*-(2-bromoethyl)phthalimide (25.4 g, 0.1 mol) in dry THF (70 ml). After completion of the addition the reaction mixture was stirred for 30 min at −40 °C and then brought to room temperature and stirred for 17 h. It was then worked up by addition of water (20 ml) and extraction with ethyl acetate (3 × 30 ml); the combined extracts were dried (Na_2SO_4), filtered, and evaporated to give a gum (18.92 g) shown by t.l.c. [ethyl acetate–cyclohexane (1:2)] to be a four-component mixture, partial separation of which was achieved by column chromatography on silica gel (ART 9385) using ethyl acetate–cyclohexane (1:4) as eluant. Three main fractions were obtained. Fraction A: 4.76 g of crude solid. Two recrystallisations from ethyl acetate–light petroleum afforded a pure product (0.67 g, 7.7%), m.p. 144—147 °C (lit.,[6] 145—146 °C). Structure (**4**) is in agreement with the analytical and spectral data. (Found: C, 82.7; H, 4.9; N, 0.1. Calc. for $C_{20}H_{14}O_2 \cdot 0.25H_2O$: C, 82.62, H, 4.99; N, 0%); $\nu_{max.}$ (KBr disc) 1 660, 1 271, 936, 772, 702, and 643 cm^{-1}; $\delta_H[(CD_3)_2SO]$ 3.36 (H_2O) and 7.25—8.00 (m); M^+, *m/z* 286.

Fraction B: 2.56 g of crude solid. Two recrystallisations from ethyl acetate–light petroleum afforded two pure compounds: *compound* (*a*) (0.262 g, 2.2%), m.p. 219.5—222 °C. Structure (**5**) is in agreement with the analytical and spectral data (Found: C, 76.8; H, 5.3; N, 5.6. $C_{16}H_{13}NO_2$ requires C, 76.49; H, 5.18; N, 5.58%); $\nu_{max.}$ (KBr disc) 3 600—2 500, 1 687, 1 640, 1 357, 1 054, 863, and 751 cm^{-1}; $\delta_H[CDCl_3–(CD_3)_2SO]$ 4.47 (1 H, d, J_{H_a,H_b} 9.8 Hz, H_b), 4.88 (1 H, d, $J_{H_a,H_{b'}}$ 16.5 Hz, $H_{b'}$), 6.84 (1 H, dd, J_{H_b,H_a} 9.6 Hz, $J_{H_{b'},H_a}$ 16.1 Hz, H_a), 7.10 (1 H, s, OH), and 7.16—7.81 (9 H, m, ArH); M^+, *m/z* 251. *Compound* (*b*) (0.162 g, 0.6%), m.p. 147—149 °C. This was identified as (**3b**) by t.l.c. comparison with the batch prepared by method A.

Fraction C: 0.72 g of crude solid. One recrystallisation from ethyl acetate–light petroleum gave a pure compound (0.45 g, 1.4%), m.p. 187—188 °C. Structure (**6**) is in agreement with analytical and spectral data (Found: C, 80.0; H, 5.9; N, 4.2. $C_{22}H_{19}NO_2$ requires C, 80.24; H, 5.78; N, 4.25%); $\nu_{max.}$ (KBr disc) 3 600—3 120, 1 662, 1 410, 1 050, 770, 750, and 698 cm^{-1}; $\delta_H(CDCl_3)$ 2.42—3.81 (5 H, m, CH_2CH_2 + OH) and 6.93—7.86 (14 H, m, ArH); M^+, *m/z* 329.

Reaction of Compound (**3b**) *with Aqueous Base.*—A solution of (**3b**) (0.168 g, 0.67 mmol) and potassium hydroxide (0.038 g, 0.67 mmol) in water–methanol (1:1; 10 ml) was refluxed for 3 h, and then worked up by addition of water (5 ml) and extraction with ethyl acetate (2 × 10 ml) to remove any unchanged starting material. The aqueous phase was acidified to pH 2—3 (conc. hydrochloric acid) and extracted with 6 × 10 ml ethyl acetate. This extract was identical [t.l.c. chloroform–methanol (8:1)] to a methanol extract obtained from the solid afforded by evaporation of the aqueous phase. The combined organic extracts were dried (Na_2SO_4) and the solvent removed to give product (0.100 g, 66%), m.p. 121—125 °C [lit.,[7] 95 °C ($1H_2O$), 127—129 °C (anhydrous)] (Found: C, 73.7; H, 4.6. Calc. for $C_{14}H_{10}O_3 \cdot \frac{1}{8}H_2O$: C, 73.69; H, 4.49%). This compound was identified as (**11**) by comparison with an authentic sample [t.l.c. in chloroform–methanol (4:1), chloroform–methanol (8:1), ethyl acetate–cyclohexane (1:1); i.r. and n.m.r. spectra. The latter also shows the presence of H_2O].

Preparation of N-(2-*Bromoethyl*)*phthalimidine* (**7**).—Sodium borohydride (2.28 g, 0.06 mol) was added portionwise to a solution or suspension of *N*-(2-bromoethyl)phthalimide (50.8 g, 0.2 mol) in methanol (300 ml). After completion of the addition the reaction mixture was stirred for 2 h at 0—5 °C and then for 22 h at room temperature under positive nitrogen pressure. Evaporation of the solvent afforded a solid (74.45 g) which was dissolved in ethyl acetate (250 ml) plus water (80 ml); the aqueous phase was separated and washed with ethyl acetate (40 ml). The combined organic phases were washed with water (40 ml), dried (Na_2SO_4), filtered, and evaporated to give a solid (36.21 g) which was recrystallised from chloroform–ether to give pure *product* (**7**) (12.64 g, 25%), m.p. 129—132 °C (Found: C, 46.6; H, 3.8; N, 5.3. $C_{10}H_{10}BrNO_2$ requires C, 46.88; H, 3.91; N, 5.47%); $\nu_{max.}$ (KBr disc) 3 240, 1 677, 1 058, and 748 cm^{-1}; $\delta_H[CDCl_3–(CD_3)_2SO]$ 3.50—3.77 (2 H, m) and 3.50—4.12 (2 H, m) [CH_2CH_2], 5.86 (1 H, d, *J* 9 Hz, collapses to singlet on addition of D_2O, *H*C-OH), 6.53 (1 H, d, *J* 9 Hz exchangeable in D_2O, OH), 7.28—7.86 (4 H, m, ArH); M^+, *m/z* 255.00 with correct isotope pattern.

Preparation of 2,3-*Dihydro*-9bH-*oxazolo*[2,3-a]*isoindol*-5(9bH)-*one* (**3c**).—Potassium t-butoxide (4.24 g, 0.038 mol) was carefully added to a refluxing solution of *N*-(2-bromoethyl)-phthalimidine (**7**) in t-butyl alcohol (40 ml) and refluxing continued for 5 h under positive nitrogen pressure. Evaporation of solvent followed by extraction of the residue with ethyl acetate (100 ml + 2 × 50 ml), filtration, and evaporation afforded a syrup which was shown by t.l.c. [chloroform–methanol (8:1)] to contain product and starting material together with minor impurities which were removed by column chromatography on silica gel [ART 9385, ethyl acetate–cyclohexane (1:3)] to give a two-component mixture which was purified by low-temperature recrystallisation from methanol to afford *product* (**3c**), (0.26 g, 3.9%), m.p. 35—39 °C (Found: C, 68.5; H, 5.1; N, 7.9. $C_{10}H_9NO_2$ requires C, 68.57; H, 5.14; N, 8.00%); $\nu_{max.}$ (KBr disc) 2 360, 1 708, 1 394, 1 032, 750, and 697 cm^{-1}; $\delta_H[(CD_3)_2SO]$ 3.33—3.58 (1 H, m) and 3.82—4.07 (1 H, m) (NCH_2), 4.07—4.50 (2 H, m, OCH_2), 5.82 (1 H, s, CH), 7.42—7.93 (4 H, m, ArH); M^+, *m/z* 175.07.

Conversion of *N*-(2-bromoethyl)phthalimide into (**3c**) without isolation of (**7**) was carried out by performing the sodium borohydride reduction with t-butyl alcohol as solvent. After the reduction was adjudged complete by t.l.c. [ethyl acetate–

cyclohexane (1:1)] 1 equiv. of potassium t-butoxide was added and the reaction mixture was refluxed for 18 h. Work-up as described above gave (**3c**) in 32% overall yield. Compound (**3c**) (0.12 g) was stirred with potassium hydroxide (0.039 g) in water (5 ml) overnight at room temperature. The mixture was extracted with ethyl acetate (2 × 5 ml), acidified to pH 1—2 (conc. HCl), and extracted further with ethyl acetate (4 × 5 ml); the extracts were dried (Na_2SO_4), filtered, and evaporated to afford a crystalline solid (42 mg, 41%) shown by t.l.c. comparison with a commercial sample to be *o*-formylphthalic acid (**10c**).

Preparation of 1-(2-*Furyl*)*phthalazin*-4(3H)-*one* (**9a**).—A solution of hydrazine hydrate (2.5 g, 50 mmol) and (**3a**) (1.2 g, 5 mmol) in ethanol (35 ml) was refluxed for 16 h. Evaporation of solvent afforded a solid which was recrystallised twice from propanol to give the *product* (**9a**) (0.17 g, 16%), decomp. 145 °C (Found: C, 67.9; H, 3.9; N, 13.35. $C_{12}H_8N_2O_2$ requires C, 67.92; H, 3.77; N, 13.21%); $\nu_{max.}$ (KBr disc) 3 500—2 000 and 1 650 cm^{-1}; $\delta_H(CDCl_3)$ 6.60 (1 H, dd, J_{H_B,H_C} 3.6 Hz, J_{H_B,H_A} 1.8 Hz, H_B), 6.95 (1 H, dd, J_{H_C,H_B} 3.6 Hz, J_{H_C,H_A} 0.8 Hz, H_C), 7.66 (1 H, dd, J_{H_A,H_B} 1.8 Hz, J_{H_A,H_C} 0.8 Hz, H_A), 7.70—8.00 (2 H, m), and 8.26—8.62 (2 H, m) (ArH); M^+, *m/z* 211.99.

Preparation of 1-*Phenylphthalazin*-4(3H)-*one* (**9b**).—A solution of hydrazine hydrate (5.0 g, 100 mmol) and (**3b**) (1.26 g, 5 mmol) in dry *N*,*N*-dimethylformamide (DMF) (10 ml) was refluxed for 20 h and the solid (**9b**) which crystallised out on cooling to room temperature was filtered off, washed with DMF, and recrystallised from propanol (0.54 g, 49%), m.p. 236—238 °C (Found: C, 75.45; H, 4.5; N, 12.5. $C_{14}H_{10}N_2O$ requires C, 75.68; H, 4.50; N, 12.61%); $\nu_{max.}$ (KBr disc) 3 500—2 500 and 1 671 cm^{-1}; δ_H [$(CO_3)_2SO$] 7.57 (5 H, s, Ph), 7.63—7.77 (1 H, m), 7.77—7.95 (2 H, m), and 8.23—8.41 (1 H, m) (ring B, ArH), one exchangeable proton at low field, (OH); M^+, *m/z* 222 and $(M-1)^+$ 221.07.

Preparation of Phthalazin-4(3H)-*one* (**9c**).—A solution of hydrazine hydrate (0.6 g, 1.2 mmol) and (**3c**) (0.21 g, 12 mmol) in ethanol (10 ml) was refluxed with exclusion of atmospheric moisture. After 38 h the reaction was incomplete as judged by t.l.c. A further quantity of hydrazine hydrate (0.6 g, 12 mmol) was added and the mixture refluxed for 12 h longer. Evaporation of solvent afforded a yellow solid which was recrystallised from ethanol (**9c**) (0.084 g, 48%), m.p. 182—183 °C (lit.,[8] 182 °C) (Found: C, 65.6; H, 4.3; N, 19.1. Calc. for $C_8H_6N_2O$: C, 65.75; H, 4.11; N, 19.18%); $\nu_{max.}$ (KBr disc) 3 300—2 000 and 1 650 cm^{-1}; $\delta_H(CDCl_3)$ 7.70—7.76 (1 H, m, 4-H), 7.76—7.80 (2 H, m, 5-H and 6-H), 8.18 (1 H, s, N=CH), 8.40—8.46 (1 H, m, 7-H), and 12.90 (1 H, br s, OH); M^+, *m/z* 146.

Preparation of o-*Di*-2-*furoylbenzene* (**12**).—A solution of 2-furyl-lithium in THF was prepared by adding n-butyl-lithium (1.7M-solution in hexane; 3 ml, 5 mmol) to a solution of furan (0.34 g, 5 mmol) in dry THF (25 ml) and stirring at 40 °C for 3 h under positive nitrogen pressure. The solution was then cooled to −40 °C and a solution of (**3a**) (1.2 g, 5 mmol) in THF (30 ml) was added during 30 min. After completion of the addition the mixture was stirred at −40 °C for 1 h followed by 23 h at room temperature; the mixture was then worked up by the addition of water (15 ml) and extraction with ethyl acetate (2 × 30 ml); the combined extracts were dried (Na_2SO_4), filtered, and evaporated to afford a brown residue (1.03 g) which was purified by column chromatography [silica gel ART 9385, ethyl acetate–cyclohexane (1:4)] to afford the product which was recrystallised from ethyl acetate to give (**12**) (0.20 g, 15%), m.p. 155.5—158 °C (Found: C, 72.1; H, 3.85. $C_{16}H_{10}O_4$ requires C, 72.18; H, 3.76%); $\nu_{max.}$ (KBr disc) 1 640, 1 590, 1 560, 1 445, 1 373, and 1 290 cm^{-1}; $\delta_H(CDCl_3)$ 6.50 (2 H, m, H_B), 7.20 (2 H, m, H_C), and 7.38—7.90 (6 H, m, H_A + ArH); M^+, *m/z* 266.10.

Preparation of 2-*Furoylbenzophenone* (**13**).—A solution of 2-furyl-lithium in THF was prepared by adding n-butyl-lithium (1.6 M-solution in hexane, 3.75 ml, 6 mmol) to a solution of furan (0.41 g, 6 mmol) in dry THF (30 ml) and stirring at 40 °C for 3 h under a positive nitrogen pressure. The solution was then cooled to −40 °C and a solution of (**3b**) (1.26 g, 5 mmol) in THF (30 ml) was added during 25 min. After completion of the addition the mixture was stirred at −40 °C for 45 min followed by 17 h at room temperature; it was then worked up by the addition of water (10 ml) and extraction with ethyl acetate (2 × 25 ml). The combined extracts were dried (Na_2SO_4), filtered, and evaporated to afford a purple gum (1.13 g) which was purified by washing through a pad of silica gel (ART 9385) with ethyl acetate–cyclohexane (1:2) (180 ml) and evaporation of solvent to give a gum which crystallised on treatment with ether–light petroleum. The solid was recrystallised from ethyl acetate–light petroleum to give the *product* (**13**) (0.13 g, 9%), m.p. 100—101 °C (Found: C, 78.0; H, 4.5. $C_{18}H_{12}O_3$ requires C, 78.26; H, 4.35%); $\nu_{max.}$ (KBr disc) 1 640, 1 455, 1 388, 1 308, and 1 277 cm^{-1}; $\delta_H(CDCl_3)$ 6.43 (1 H, dd, J_{H_B,H_C} 3.5 Hz, J_{H_B,H_A} 1.7 Hz, H_B), 7.02 (1 H, dd, J_{H_C,H_B} 3.5 Hz, J_{H_C,H_A} 0.7 Hz, H_C), and 7.20—7.80 (10 H, m, H_A + ArH); M^+, *m/z* 276.04.

Preparation of o-*Dibenzoylbenzene* (**4**).—To a solution of phenyl-lithium [1.9M in cyclohexane–ether (7:3); 2.63 ml, 0.005 mol] diluted with dry THF (35 ml) and cooled to −40 °C with stirring was added during 35 min under a positive nitrogen pressure a pre-cooled solution of (**3b**) (1.26 g, 5 mmol) in THF (25 ml). After completion of the addition the mixture was stirred at −40 °C for 20 min and then allowed to warm to 13 °C during 5 h before being worked up by addition of water (10 ml) and extraction with ethyl acetate (3 × 20 ml). The combined extracts were dried (Na_2SO_4), filtered, and evaporated to give a solid (**4**) which was recrystallised from ethyl acetate–light petroleum (0.79 g, 55%). T.l.c. comparison [ethyl acetate–cyclohexane (1:2)] with the sample obtained by the alternative route previously described identified the product as (**4**).

Preparation of 1,4-*Diphenylphthalazine* (**14**).—A solution of hydrazine hydrate (0.017 g, 0.34 mmol) and (**4**) (0.050 g, 0.17 mmol) in ethanol (6 ml) was stirred for 17 h at room temperature. Evaporation of solvent gave a solid which was recrystallised from ethyl acetate–light petroleum to give (**14**) (0.032 g, 67%), m.p. 190—192 °C (lit.,[9] 192 °C) (Found: C, 84.9; H, 5.2; N, 9.7. Calc. for $C_{20}H_{14}N_2$: C, 85.11; H, 4.96; N, 9.93%); $\nu_{max.}$ (KBr disc) 3 070, 1 400, and 1 379 cm^{-1}; δ_H [$CDCl_3$–$(CD_3)_2SO$ (1:1)] 7.50—8.15 (m, ArH).

Preparation of 1,4-*Di*-2-*furylphthalazine* (**15**).—A solution of hydrazine hydrate (0.020 g, 0.4 mmol) and (**11**) (0.053 g, 0.2 mmol) in ethanol (2 ml) was refluxed for 14 h. Evaporation of solvent gave a gum (**15**) which solidified on scratching (0.011 g, 21%), m.p. 114.5—115.5 °C (Found: C, 73.0; H, 4.0; N, 10.4. $C_{16}H_{10}N_2O_2$ requires C, 73.28; H, 3.82; N, 10.69%); $\nu_{max.}$ (KBr disc) 3 115 and 1 477 cm^{-1}; $\delta_H(CDCl_3)$ 6.70 (2 H, dd, J_{H_B,H_C} 3.5 Hz, J_{H_B,H_A} 1.7 Hz, 2 H_B), 7.50 (2 H, dd, J_{H_C,H_B} 3.5 Hz, J_{H_C,H_A} 0.9 Hz, 2 H_C), 7.77 (2 H, dd, J_{H_A,H_B} 1.7 Hz, J_{H_A,H_C} 0.9 Hz, 2 H_A), 7.86—8.00 (2 H, m), and 8.84—9.00 (2 H, m) (Ph); M^+, *m/z* 262.

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