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APPLICATION OF ORGANOLITHIUM AND RELATED REAGENTS IN SYNTHESIS. PART 13[1]. SYNTHETIC STRATEGIES BASED ON AROMATIC METALLATION. A CONCISE REGIOSPECIFIC CONVERSION OF BENZOIC ACIDS INTO 4-HYDROXY-1-ARYLNAPHTHALENES

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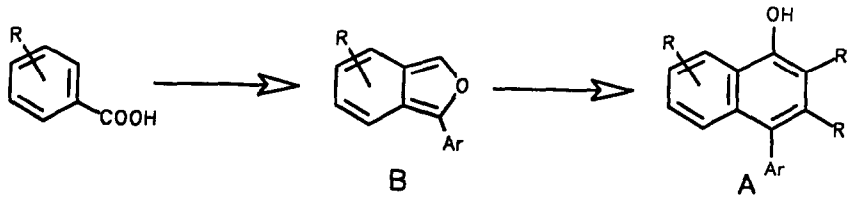
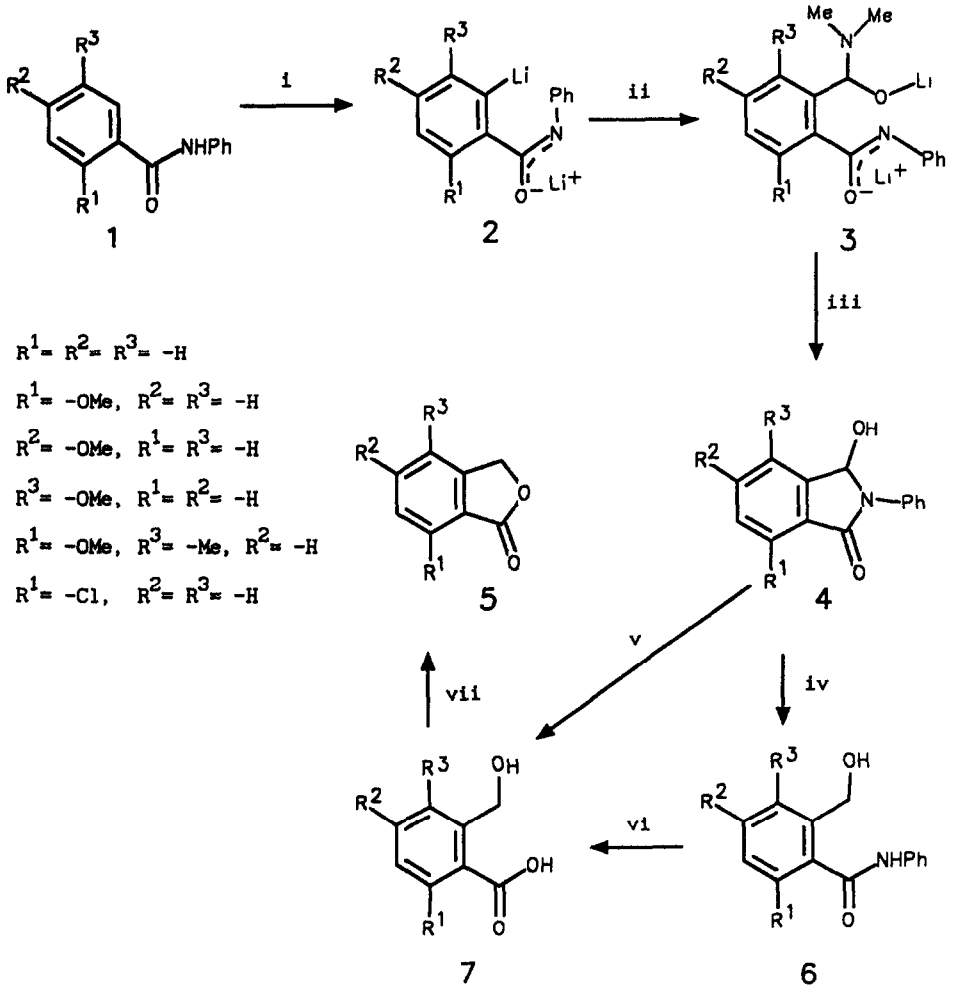
Abstract The synthesis of the 3-unsubstituted phthalides (5) and their conversion into 1-hydroxy-1-arylphthalans (8), very useful precursors of isobenzofurans (10) and subsequent cycloaddition of them to dimethyl acetylenedicarboxylate as a way of regiospecific transformation of benzoic acids into dimethyl 4-hydroxy-1-(2-methoxyphenyl)naphthalene-2,3-dicarboxylates (12) (biaryls highly substituted around the axis), is described

In the past few years we have witnessed a tremendous activity directed towards the synthesis of the naturally occurring biaryls The biaryl axis is the central building block in a very large number of natural products of different structure, biological activity, and biosynthetic origin including, for example, polyketides, terpenes, lignans, coumarins, flavonoids, tanins, peptides and alkaloids[2] In particular, our attention have been focussed on the having synthetic methodology for the preparation of biaryls (**A**), which are used to be readily prepared via Diels-Alder reaction of dienophiles with 1-aryl-isobenzofurans (**B**)[3,4,5,6,7] This has promoted us to investigate the regiospecific synthesis of the 1-hydroxy-1-arylphthalans ⇄ *ortho*-hydroxymethylbenzophenones (ring -



chain tautomers of the keto - lactol type), that are, by far, the most popular and useful precursors for the generation of the isobenzofurans (IBF)[4,5,6,7]

We now describe herein an efficient synthetic sequence, as a general strategy, for the transformation of benzoic acids into 4-hydroxy-1-arylnaphthalenes (A) (biaryls highly substituted around the axis) via Diels-Alder addition of dimethyl acetylenedicarboxylate (DMAD) to the corresponding IBFs (B)



i, nBuLi in THF, -78°C (0 5 h) → 0°C (0 1 h), ii, Me_2N-CHO, -78°C (1 h) → 20°C (1 h), iii, hydrolytic workup, iv, KBH_4 in MeOH, 20°C, v, Zn - LiOH, vi, 15% HCl, 20°C, vii, $H^{\oplus}$

Basing on the reports[4,5,6,7] that the phthalides as an ortho substituted benzenoid starting materials, which are conceptually and operationally simple, extremely versatile compounds for the preparation of the 1-hydroxyphthalans, at first, efficient route for the synthesis of the 3-unsubstituted phthalides, appeared to be needful

Since the classical work by Wislicenus[8] and Gabriel[9], several methods for the synthesis of phthalides have been reported These include preparation of phthalides by the oxidation of o-methylbenzoic acids[10], the oxidation of polymethylbenzonitriles with nitric acid[11], by appropriate transformations of suitable *ortho*-lithiated benzylalcohols, N,N-dialkyl-benzylamines or benzamides[12,13,14,15,16,17,18], the reduction of phthaldehydic acids prepared from o-bromobenzaldehydes[19], and recently *via* a regioselective single or double β-scission of the alkoxy radicals generated by the photolysis of the hypoiodides of 1-ethylbenzocyclo-buten-1-ols[20]

In this paper we give a full account of a new, versatile and inexpensive (readily available starting materials) route to the 3-unsubstituted phthalides The method involves the regioselective lithiation (nBuLi) - electrophilic substitution (Me_2N-CHO) sequence of the benzanilides leading to the 3-hydroxy-isoindolin-1-ones, and their subsequent reductive transformation into the phthalides

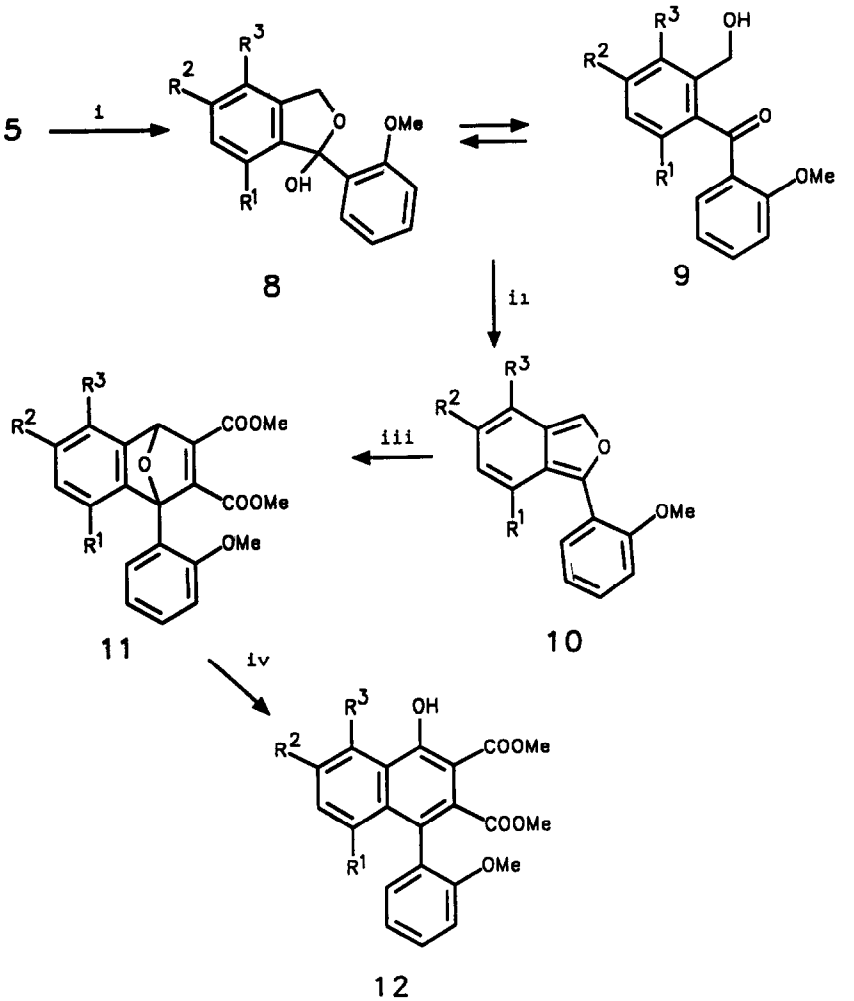
The anilides (**1**) reacted in THF with 2 1 mole equivalents of nBuLi (amide/-78°C/nBuLi/ 0 5 h → 0°C/2 h) were efficiently converted into the bis-(N- and C-*ortho*)lithiated-anilides (**2**) The treatment of the solutions of the lithiated species with dimethylformamide (DMF) afforded the corresponding formylated derivatives (**3**), which upon hydrolytic workup spontaneously cyclized into the 3-hydroxy-isoindolin-1-ones (**4**)

Our first approach to the preparation of the 3-unsubstituted phthalides was based on the reduction of the isoindolinones (**4**) with KBH_4 in MeOH and subsequently the acidic - driven cyclization of the formed hydroxymethyl-anilides (**6**) into the phthalides (**5**) It was found that the isoindolinones (**4a**), (**4b**), (**4c**) and (**4f**) on the treatment with KBH_4 in MeOH gave with a good yield the hydroxymethyl-anilides (**6a**), (**6b**), (**6c**) and (**6f**) The isoindolinones (**4d**) and (**4e**) appeared to be inert towards this reaction The hydroxymethyl-anilides (**6a**), (**6b**), (**6c**) and (**6f**) on acid - driven cyclization (15% - hydrochloric acid at room temperature) yielded the corresponding phthalides (**5a**), (**5b**), (**5c**) and (**5f**) In the case of the conversion of (**6b**) into (**5b**) the process gave a rather low yield

The encountered difficulties in the conversion of the isoindolinones (**4d**) and (**4e**) into the phthalides (**5d**) and (**5e**), and the low yield in the case of (**4b**) into (**5b**), provoked wide - spread interest in searching for a suitable procedure for this transformation It was presumed that $CuSO_4$ - activated Zn in the basic medium would be effective in this process

With this strategy in mind, $CuSO_4$ - activated Zn in LiOH for the reductive cleavage of the isoindolinones (**4**) was attempted, and indeed the phthalides (**5**) via acids (**7**),

were obtained in good yields In each case, with one exception this process gave a single product In the case of the isoindolinone (4c) the formed phthalide (5c) was accompanied by the acid (7c) Thereby, in order to improve the phthalide (5c) preparation, acidic cyclization (H_2SO_4 in boiling benzene) of the acid (7c), was requisited additionally The reductive cleavage (Cu - Zn/LiOH) of the isoindolinone (4f) produced the phthalide (5f) with some amount of (5a) This indicated that the process was accompanied by the dechlorination reaction



i, o-Methoxyphenyllithium in THF, -78°C, ii, CF_3COOH (cat) in CH_2Cl_2, 20°C, iii, MeOOC-C≡C-COOMe in CH_2Cl_2, 20°C, iv, Tos-OH (cat) in boiling benzene

The phthalides (5) reacted in THF with 1 1 mole equivalents of o-methoxyphenyllithium (prepared *via* reaction of o-bromoanizole with nBuLi[21]) were converted into the corresponding phthalans (8) ⇄ o-hydroxymethylbenzophenones (9) tautomeric mixture

While these compounds readily dehydrated, they were isolated by using mild non acidic conditions Attempts to isolate the products derived from the reaction of the phthalides (5) with o-methoxyphenyllithium as the solid samples appeared to be successful only in the case of (5a) and (5d) The infrared spectra of solid samples indicated that the (5a) gave o-hydroxymethylbenzophenone (9a) (the C=O stretch at 1650 cm^{-1}), on the other hand, (5d) was converted into phthalane (8d) (no band in the C=O stretching region) In contrast, the infrared spectra of chloroform solution of the formed compounds derived from (5a) and (5d) showed in the C=O stretching region the corresponding bands at 1650 cm^{-1} and 1655 cm^{-1}, respectively Clearly, in solution, the equilibria (8a) ⇄ (9a) and (8d) ⇄ (9d) existed The position of these equilibria was evaluated quantitatively by analysis of the ^1H - NMR spectra of deuterochloroform solutions of the compounds and it appeared to be 10 90 and 60 40, respectively (see Experimental for the specific analysis of each compound)

The tautomeric mixtures (8) ⇄ (9) without purification (in the typical procedure) on exposition to the acidic catalysis (CF_3COOH/CH_2Cl_2) generated IBFs (10), which subsequently were trapped with DMAD to give the adducts (11) The adducts (11) upon heating in benzene, in the presence of Tos-OH, gave the desired 4-hydroxy-1-arylnaphthalenes (12) in an overall good yield

The described methodology relating to the introduction of the formyl group at the *ortho* position to the anilide function of the benzoic acids, and then reductive cleavage of the formed 3-hydroxy-2-phenylisoindolin-3-ones shows considerable versatility for the regiospecific synthesis of the 3-unsubstituted phthalides This, coupled with the effective conversion of the phthalides into the corresponding isobenzofurans, which on cycloaddition process should allow the access to a wide variety of 1-aryl-4-hydroxynaphthalenes (biaryls highly substituted around the axis)

Experimental

Melting points were determined using a Boetius hot-stage apparatus and are uncorrected IR spectra were recorded on a Zeiss-Jena Specord 71-IR ^1H-NMR spectra were determined on a Tesla BS-467 (60 MHz) or a Varian-Gemini-200 (200 MHz) using TMS as an internal standard *n*-Butyllithium (*n*-BuLi) (Aldrich) was used without further purification Tetrahydrofuran (THF) was dried over calcium hydride and used directly after distillation from sodium

Benzanilides (1)

Benzanilides (**1a**), (**1b**), (**1c**), (**1d**) and (**1f**) were prepared by the standard methods

2-Methoxy-5-methylbenzanilide (**1e**)

To the stirred THF (100 ml) solution of 2-Bromo-1-methoxy-4-methylbenzene (prepared by bromination of 4-methylanisole[22]) (20 1 g 0 1 mole) *n*-BuLi (0 1 mole) at -78°C was added. The solution was kept at -78°C for 0 5 h, then allowed to rise to 0°C The whole lot was cooled to -78°C and phenyl isocyanate (11 9 g, 0 1 mole) was added. The reaction after 1h at -78°C was allowed to reach an ambient temperature, and kept for 1 h, and then water (20 ml) was added The organic layer was separated and the water layer was extracted with $CHCl_3$ The combined organic solutions were dried with magnesium sulfate and evaporated to give the crude product Recrystallization from hexane 3 ethyl acetate 2 mixture gave *2-methoxy-5-methylbenzanilide* (**1e**) (m p 91-94°C, 14,9 g, yield 62%) (Found C, 74 66, H, 6 28, N, 5 77 Calc for $C_{15}H_{15}NO_2$: C, 74 66, H, 6 27, N, 5 81%). IR (KBr) 3350 cm^{-1} (NH), 1660 cm^{-1} (C=O). ^1H NMR ($CDCl_3$, 60 MHz) 9 8 (1H, s, NH-H), 8 2-6 5 (8H, m, Ar-H), 3.8 (3H, s, OMe-H), 2 2 (3H, s, Me-H)

Preparation of 3-hydroxy-2-phenyl-2,3-dihydro-1H-isoindol-1-ones (4)

To the anilide (0 02 mole) stirred in THF (90 ml) at -78°C *n*-Buli (0 042 mole) was added The solution was held at -78°C for 0 5 h, then allowed to rise to 0°C and kept at 0°C for 0 1 h The whole lot was cooled to -78°C and DMF (0 04 mole) was added The reaction after 1 h at -78°C was warmed up to room temperature, and kept for 1 h, and then water (25 ml) was added The mixture was adjusted to pH ≅ 2 with hydrochloric acid and the organic layer was separated The water layer was extracted with mixture $CHCl_3$ 1 THF 1. The combined organic solutions were dried with magnesium sulfate and evaporated to give the crude products The products were purified by crystallization

3-Hydroxy-2-phenyl-2,3-dihydro-1H-isoindol-1-one (**4a**),
(82%) m p 169-170°C (methanol), (lit [23], m p 167-168°C)

3-Hydroxy-7-methoxy-2-phenyl-2,3-dihydro-1H-isoindol-1-one (**4b**),
(70%) m p 148-150°C (methanol), (lit [23], m p 147-148 C°)

3-Hydroxy-5-methoxy-2-phenyl-2,3-dihydro-1H-isoindol-1-one (**4c**),
(75%) m p 194-196°C (benzene), (Found C, 70 84, H, 5 07, N, 5 50 Calc for $C_{15}H_{13}NO_3$ C, 70 58; H, 5 13, N, 5 49%), IR (KBr) 3500-3300 cm^{-1} (OH), 1675 cm^{-1} (C=O), ^1H NMR (DMSO-d_6, 60 MHz) 8 0-7 1 (8H, m, Ar-H), 6 9 (1H, s, OH-H), 6,3 (1H, s, CH-H), 3.8 (3H, s, OMe-H)

3-Hydroxy-4-methoxy-2-phenyl-2,3-dihydro-1H-isoindol-1-one (**4d**),
(75%) m p. 167-169°C (methanol), (Found C, 70 61, H, 5 13, N, 5 45 Calc for $C_{15}H_{13}NO_3$ C, 70 58, H, 5 13, N, 5 49%), IR (KBr) 3600-3000 cm^{-1} (OH), 1680 cm^{-1} (C=O), ^1H NMR (DMSO-d_6, 60 MHz) 7 9-7 8 (8H, m, Ar-H), 6 7-6 1 (2H, m, OH-H and CH-H), 3 7 (3H, s, OMe-H)

3-Hydroxy-7-methoxy-4-methyl-2-phenyl-2,3-dihydro-1H-isoindol-1-one (**4e**),
(30%) m p 202-206°C (ethanol), (Found C, 71 19, H, 5 67, N, 5 21 Calc. for $C_{16}H_{15}NO_3$ C, 71 36, H, 5 62, N, 5.20%), IR (KBr) 3600-3250 cm^{-1} (OH), 1680 cm^{-1} (C=O); ^1H NMR (DMSO-d_6, 60 MHz) 7 9-6 9 (7H, m, Ar-H), 6 5 (1H, s, OH-H), 6 4 (1H, s, CH-H), 3 8 (3H, s, OMe-H), 2 4 (3H, s, Me-H)

4-Chlor-3-hydroxy-2-phenyl-2,3-dihydro-1H-isoindol-1-one (**4f**),
(82%) m p 150-154°C (benzene), (lit [18], m p 154-156°C)

Preparation of Hydroxymethyl-benzanilides (6a, 6b, 6c and 6f) and Their Subsequent Cyclization into Phthalides (5a, 5b, 5c and 5f)

a) Reduction of isoindolinones (4a, 4b, 4c and 4f)

To the compound (**4a**), (**4b**), (**4c**) or (**4f**) (0 03 mole) in methanol (25 ml), potassium borohydride (0 07 mole) was added and the whole lot was stirred overnight at room temperature Methanol was evaporated, and to the residue water (70 ml) was added The insoluble crude products were separated and purified by crystallization

2-Hydroxymethylbenzanilide (**6a**),
(67%) m p 140-143°C (ethanol), (Found C, 74 26, H, 5.90, N, 6.18 Calc. for $C_{14}H_{13}NO_2$. C, 73,99, H, 5 77, N, 6 16%), IR (KBr) 3450-3140 cm^{-1} (NH and OH), 1640 cm^{-1} (C=O); ^1H NMR (DMSO-d_6, 60 MHz) 10 4 (1H, s, NH-H), 7 9-6 6 (9H, m, Ar-H), 5 3 (1H, br s, OH-H), 4 7 (2H, s, CH_2-H)

2-Hydroxymethyl-6-methoxybenzanilide (**6b**),
(75%) m p 187-189°C (ethanol), (Found C, 70 22, H, 5 90, N 5 35 Calc for $C_{15}H_{15}NO_3$ C, 70 02, H, 5 88, N, 5 44%), IR (KBr) 3400-3100 cm^{-1} (NH and OH), 1650 cm^{-1} (C=O), ^1H NMR (DMSO-d_6, 60 MHz) 10 2 (1H, br s, NH-H), 7 9-6 6 (8H, m, Ar-H), 5 1 (1H, br s, OH-H), 4 4 (2H, s, CH_2-H), 3 7 (3H, s, OMe-H)

2-Hydroxymethyl-4-methoxybenzanilide (**6c**),
(75%) m p 175-178°C (ethanol), (Found. C, 70 12, H, 5 87, N, 5 46 Calc for $C_{15}H_{15}NO_3$ C, 70 02, H, 5 88, N, 5 44%), IR (KBr) 3500-3150 cm^{-1} (NH and OH), 1650 cm^{-1} (C=O), ^1H NMR (DMSO-d_6, 60 MHz) 10 2 (1H, s, NH-H), 7 8-6 6 (8H, m, Ar-H), 5 3 (1H, t J 6Hz, OH-H), 4 6 (2H, d J 6Hz, CH_2-H), 3 7 (3H, s, OMe-H)

6-Chlor-2-hydroxymethylbenzanilide (**6f**),
(66%) m p 142-145°C (benzene), (Found C, 64 35, H, 4 71, N, 5 28, Cl, 13 59 Calc for $C_{14}H_{12}ClNO_2$ C, 64 24, H, 4 62, N, 5 35, Cl, 13 56%), IR (KBr) 3500-3150 cm^{-1} (NH and OH), 1650 cm^{-1} (C=O), ^1H NMR (DMSO-d_6, 200 MHz) 10 40 (1H, s, NH-H), 8 00-7 00 (8H, m, Ar-H), 5 20 (1H, t J 5 2Hz, OH-H) 4 64 (2H, d J 5 2Hz, CH_2-H)

b) Cyclization

To hydrochloric acid (15%, 20 ml) the compound (**6a**), (**6b**), (**6c**) or (**6f**) (0.005 mole) was added and the whole lot was kept at room temperature for 3 days Then the mixture was heated under reflux for 2 minutes, and cooled

In the case of the phthalides (**6a**) or (**6b**) the obtained solution was continuously extracted with $CHCl_3$ and the extract was dried with magnesium sulfate The solvent was evaporated and the residue was purified by crystalization In the case of (**6c**) or (**6f**)

the insoluble product was separated and purified by crystalization
Phthalide (**5a**), (61%) m p 70-73°C (water), (lit [24], m p 72-73°C)
7-Methoxyphthalide (**5b**), (35%) m p 107-109°C (ethyl acetate 1 hexane 1), (lit [25], m p 108°C)
5-Methoxyphthalide (**5c**), (75%) m p 117-118°C (ethanol), (lit [26], m p 119°C)
7-Chlorphthalide (**5f**), (68%) m p 140-144°C (ethanol), (lit [18], m p 142-144°C)

Reductive Cleavage of Isoindolinones (4a, 4b, 4c, 4d and 4e) with Zinc - Lithium Hydroxide System into Phthalides (5a, 5b, 5c, 5d and 5e)

The suspension of freshly prepared Zn - Cu couple [prepared from commercial Zn dust (3 g) and $CuSO_4$ (0 1 g) in water (10 ml)], $LiOH \cdot H_2O$ (4 2 g, 0 1 mole) and the isoindolinones (**4**), in the case of (**4a**), (**4b**), (**4c**) and (**4d**) in water (30 ml), while, in the case of (**4e**) in the mixture of 1-propanol - water (1 1, 30 ml), were heated till boiling for 1 h [50 h in the case of (**4e**)] The formed aniline was removed by steam distillation and water (50 ml) was added, and then the excess of zinc was filtered off In the case of isoindolinone (**4e**) before addition of water, aniline and 1-propanol were removed in vacuum The filtrates were adjusted to pH ≅ 1 with hydrochloric acid, and the precipitated phthalides (**5**) were filtered, and purified by crystallization In the case of the conversion of (**4e**) into (**5e**), the formed phthalide was accompanied by the acid (**7e**) as the material insoluble in $CHCl_3$ The acid (**7e**) heated till boiling in benzene with a drop of H_2SO_4 for 0 5 h under Dean - Stark trap, gave the phthalide (**5e**) in quantitative yield
Phthalide (**5a**), (83%) m p 70-72°C (water), (lit [24], m p 72-73°C)
7-Methoxyphthalide (**5b**), (60%) m p 107-109°C (ethyl acetate 1 hexane 1), (lit [25], m p 108°C)
5-Methoxyphthalide (**5c**), (75%) m p 117-118°C (ethanol), (lit [26], m p 119°C)
4-Methoxyphthalide (**5d**), (75%) m p 126-128°C (ethanol), (lit. [27], m p 127°C)
7-Methoxy-4-methylphthalide (**5e**), (68%) m p 140-142°C (sublimation), (Found C, 67 61, H, 5 56 Calc for $C_{10}H_{10}O_3$ C, 67 40, H, 5 66%), IR (KBr) 1750 cm^{-1} (C=O), ^1H NMR ($CDCl_3$, 200 MHz) 7 38 (1H, d J 8 2Hz, 5-H), 6 85 (1H, d J 8 2Hz, 6-H), 5 15 (2H, s, 3-H), 3 96 (3H, s, OMe-H), 2 24 (3H, s, Me-H)

Dimethyl 4-hydroxy-1-(2-methoxyphenyl)naphthalene-2,3-dicarboxylates (12)

a) Addition of 2-methoxyphenyllithium to phthalides (5a, 5b, 5c, 5d and 5f)

To the stirred THF (70 ml) solution of phthalides (**5a-d** and **5f**) (0 01 mole) 2-methoxyphenyllithium (0 01 mole) (2-methoxyphenyllithium was obtained according to a known procedure[21], dissolved in THF and titrated before use) at -78°C was added The solution was held at -78°C for 0 5 h, then allowed to rise to 20°C and kept at 20°C for 0 5 h The solvents were evaporated in vacuum, water (30 ml) was added and the whole lot was extracted with $CHCl_3$ The organic solution was dried with magnesium sulfate and evaporated to give the crude products, which were used without further purification for generation of isobenzofuranes In the case of the products formed from the phthalides (**5a**) and (**5d**) solid samples were isolated For consistency with ring - chain tautomerism, the structures of isolated compounds were assigned following conclusions from the

infrared spectra in nujol

1-Hydroxymethyl-2'-methoxybenzophenone (**9a**), (88%) m p 90-92°C (benzene), (Found C, 74 42, H, 5 89 Calc for $C_{15}H_{14}O_3$ C, 74 36, H, 5 38%), IR (nujol) 3520 cm^{-1} (OH), 1650 cm^{-1} (C=O), The IR data suggested that in solid state this compound existed in the form (**9a**) but in solution mixture of two isomers (**9a**) and (**8a**) *[1,3-dihydro-1-(2-methoxyphenyl)-1-isobenzofuranol]* was observed ^1H NMR ($CDCl_3$, 60 MHz, 20°C) 7 8-6 6 (8H, m, Ar-H **9a** and **8a**), 5 9 (0 1H, s, OH-H **8a**), 5 3 and 5 0 (0 2H, two d J 12Hz, CH_2-H **8a**), 4 7 (1 8H, d J 8Hz, CH_2-H **9a**), 4 0 (0 9H, t J 8Hz, OH-H **9a**), 3 8 (0 3H, s, OMe-H **8a**), 3 5 (2 7H, s, OMe-H **9a**)

1,3-Dihydro-4-methoxy-1-(2-methoxyphenyl)-1-isobenzofuranol (**8d**), (45%) m p 95-98°C (benzene 1 hexane 1), (Found C, 70 43, H, 5 72 Calc for $C_{16}H_{16}O_4$ C, 70 54, H, 5 92%), IR (nujol) 3350 cm^{-1} (OH), (no carbonyl absorption bond), The IR data suggested that in solid state this compound existed in the isobenzofuranol form (**8d**) but in solution mixture of two isomers (**8d**) and (**9d**) *[2-Hydroxymethyl-3,2'-dimethoxybenzophenone]* was observed, ^1H NMR ($CDCl_3$, 60MHz) 7 6-6 6 (7H, m, Ar-H **8d** and **9d**), 5 8 (0 6H, s, OH-H **8d**), 5 3 and 5 0 (1 2H, two d J 12Hz, CH_2-H **8d**), 4 7 (0 8H, d J 8Hz, CH_2-H **9d**), 4 0-3 3 (6 4H, four s, OMe-H **8d**, **9d** and OH-H **9d**)

b) Diels - Alder Reaction

To the crude tautomeric mixture derived from the addition of 2-methoxyphenyllithium to the phthalides and dimethyl acetylenedicarboxylate (0 04 mole), a catalytic amount of trifluoroacetic acid was added The mixtures were keptat room temperature overnight The solvent was evaporated and the excess of dimethyl acetylenedicarboxylate was separated by column chromatography (silica gel, benzene and next chloroform) and the products were aromatizated by reflux (4h) with catalytic amount of *p*-toluenesulfonic acid in dry benzene To the whole lot water (5 ml) was added The organic layer was separated and evaporated to give the crude product which was purified by crystalization The product in the case of phthalide (**5c**) was separated by column chromatography (silica gel, $CHCl_3$) and purified by crystalization

Dimethyl 4-hydroxy-1-(2-methoxyphenyl)naphthalene-2,3-dicarboxylate (**12a**), (45%), 165-167°C (benzene 1 hexane 4), (Found C, 68 80, H, 4 91 Calc for $C_{21}H_{18}O_6$ C, 68 84, H, 4 95%), IR (KBr) 1740 cm^{-1} and 1670 cm^{-1} (C=O), ^1H NMR ($CDCl_3$, 60 MHz) 12 4 (1H, s, OH-H), 8 5-8 3 (1H, m, 5-H), 7 8-6 7 (7H, m, Ar-H), 3 8 (3H, s, OMe-H), 3 6 (3H, s, OMe-H), 3 4 (3H, s, OMe-H)

Dimethyl 4-hydroxy-8-methoxy-1-(2-methoxyphenyl)naphthalene-2,3-dicarboxylate (**12b**), (33%), 183-185°C (benzene 1 hexane 1), (Found C, 66 63, H, 5 08 Calc for $C_{22}H_{20}O_7$ C, 66 66, H, 5 09%), IR (KBr) 1750 cm^{-1} and 1650 cm^{-1} (C=O), ^1H NMR ($CDCl_3$, 60 MHz) 12 4 (1H, s, OH-H), 8 1 (1H, dd J 8 and 1Hz, 5-H), 7 7-6 6 (6H, m, Ar-H), 3 8 (3H, s, OMe-H), 3 6 (3H, s, OMe-H), 3 4-3 3 (6H, two s, OMe-H)

Dimethyl 4-hydroxy-6-methoxy-1-(2-methoxyphenyl)naphthalene-2,3-dicarboxylate (**12c**), (45%), 202-205°C (benzene), (Found C, 65 93, H, 5 02 Calc for $C_{22}H_{20}O_7$ C, 66.66, H, 5 09%), IR (KBr) 1730 cm^{-1} and 1670 cm^{-1} (C=O), ^1H NMR ($CDCl_3$, 200 MHz) 12 33 (1H, s, OH-H), 7 76 (1H, d J 2 2Hz, 5-H), 7 40-6 90 (6H, m, Ar-H), 3 97 (3H, s, OMe-H), 3 93 (3H, s, OMe-H), 3 68 (3H, s, OMe-H), 3 51 (3H, s, OMe-H)

Dimethyl 4-hydroxy-5-methoxy-1-(2-methoxyphenyl)naphthalene-2,3-dicarboxylate (**12d**), (48%), 150-153°C (benzene 1 hexane 1), (Found C, 66 82, H, 5 31 Calc for $C_{22}H_{20}O_7$ C, 66 66, H, 5 09%), IR (KBr) 1730 cm^{-1} and 1660 cm^{-1} (C=O), ^1H NMR ($CDCl_3$, 60 MHz) 11 6 (1H, s, OH-H), 7,2-6 6 (7H, m, Ar-H), 4 0 (3H, s, OMe-H), 3 8 (3H, s, OMe-H), 3 6 (3H, s, OMe-H), 3 4 (3H, s, OMe-H)

Dimethyl 8-chlor-4-hydroxy-1-(2-methoxyphenyl)naphthalene-2,3-dicarboxylate (**12f**), (61%), m p 151-153°C (benzene 1 hexane 1), (Found C, 62 92, H, 4 28, Cl, 8 69 Calc for $C_{21}H_{17}ClO_6$ C, 62 93, H,4 27, Cl, 8 85%), IR (KBr) 1730 cm^{-1} and 1670 cm^{-1} (C=O), ^1H NMR ($CDCL_3$, 60 MHz) 12 5 (1H, s, OH-H), 8 5 (1H, dd J 8 and 2Hz, 5-H), 7 8-6 7 (6H, m, Ar-H), 3 8 (3H, s, OMe-H), 3 6 (3H, s, OMe-H), 3 3 (3H, s, OMe-H)

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