Superacid-catalysed arylation and rearrangement in 2-hydroxy-2,2'-biindan-1,1',3,3'-tetrone and facile synthesis of 4-substituted phthalazinones

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2-Hydroxy-2,2′-biindan-1,1',3,3'-tetrone **1** upon stirring with moderately activated and deactivated arenes in superacidic triflic acid (CF_3SO_3H, TfOH) medium produces arylated adducts 2-aryl-2,2'-biindan-1,1',3,3'-tetrones **3** within 1-2 h. Prolonged stirring (12–24 h) of the same reaction mixture gives rearranged products 3-(aryl-1,3-indanedionylmethylene)isobenzofuranones **4** involving three types of regioselectivity. The arylated adducts **3** and rearranged products **4** undergo nucleophilic ring opening and condensation with hydrazine hydrate to produce 4-substituted mono- and diphthalazinones depending upon the reaction temperature.

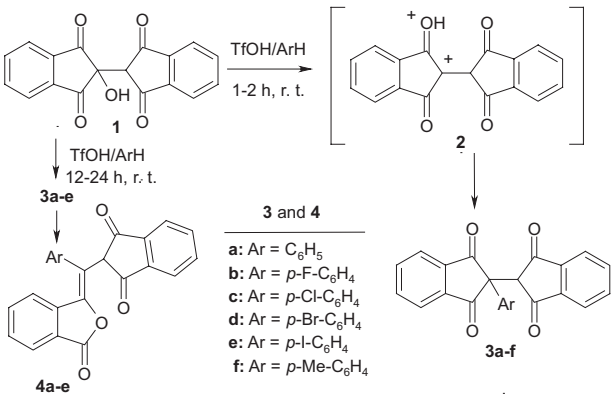
Keywords: 2-hydroxy-2,2'-biindan-1,1',3,3'-tetrone, superacid, isobenzofuranones, phthalazinones, hydrazine hydrate

The acid-catalysed condensation of 2-hydroxy-2,2'-biindan-1,1',3,3'-tetrone **1** with activated aromatics has been studied recently.[1] However, condensation of **1** with moderately activated and deactivated aromatics such as benzene, toluene and halobenzenes has not been studied yet. Several reports have appeared where superacidic triflic acid (CF_3SO_3H, TfOH) has been exploited to carry out electrophilic chemistry of 1,2- and 1,3-dicarbonyl compounds including ninhydrin,[2,3] but the electrophilic chemistry of **1,** a structurally complex system remains totally unexplored. We now report an extensive study of the electrophilic chemistry of **1** in a superacid medium. This study also creates an opportunity for exploring the synthetic aspects of tetrones in heterocyclic chemistry.

Generally 4-substituted (2*H*)-phthalazinones are found to possess important biological activities such as antibacterial,[4] antifungal,[4] antidiabetic[5] and antiallergic activities.[6] They are also suitable intermediates for the synthesis of inhibitors of the VEGF (vascular endothelial growth factor)-receptor tyrosine kinases which are utilised for the treatment of cancer.[7] Phthalazinone derivatives can play important role in the development of antiasthmatic agents with the dual activities of thromboxane A_2 (TXA_2) synthetase inhibitor and bronchodilation.[8] The phthalazinone nucleus has been proved to be a versatile system in medicinal chemistry. Various derivatives of it are well recognised pharmacophores that show a wide range of biological activities. Despite the useful nature of phthalazinones, there are only a limited number of synthetic approaches available[9] and, therefore, synthesis and functionalisation of phthalazinones continues to be of interest. We now report an efficient and general method for the preparation of a new class of potentially bio-active and structurally complex 4-substituted (2*H*)-phthalazinones starting from an easily achievable tetrone.

Results and discussion

In the present study, it has been observed that moderately activated and deactivated aromatics such as benzene, toluene, halobenzenes condense smoothly with **1** in superacidic triflic acid medium within 1–2 h (Scheme 1, Table 1). The condensation products **3a–f** are formed regioselectively, exclusively *para* to the substituents. ^1H and ^{13}C NMR spectra of the adducts **3a–f** display a symmetrical pattern for two 1,3-dioxoindane moieties indicating a tetraketo structure with a plane of symmetry. X-ray crystal structures of **3b** and **3f**, derived from fluorobenzene and toluene respectively, show the formation of symmetrical adducts (Figs 1 and 2).[10] In superacid medium **1** reacts with deactivated arenes such as fluoro- and chloro-benzene to produce the arylated adducts **3b** and **3c**, in good yields (Table 1). These results indicate that in superacid medium, **1** generates some reactive electrophiles such as **2** which then carry out normal electrophilic substitution to give **3a–f** (Scheme 1).



Scheme 1

Table 1 Formation of adducts **3a–f** and rearranged products **4a–e** from **1**

Arenes		Adducts **3**			Rearranged products **4**		
		Yield/%[a]	M.p./°C[b]		Yield/%[a]	Time/h	M.p./°C[b]
Benzene	**3a**	80	238–239	**4a**	60	20	266–267
Fluorobenzene	**3b**	82	191–192	**4b**	67	12	239–240
Chlorobenzene	**3c**	82	202–203	**4c**	65	12	210–211
Bromobenzene	**3d**	80	189–190	**4d**	52	20	209–210
Iodobenzene	**3e**	78	205–206	**4e**	50	24	223–224
Toluene	**3f**	82	230–231	—	—	—	———

[a]Yields refer to pure isolated products. [b]M.p.s are uncorrected.

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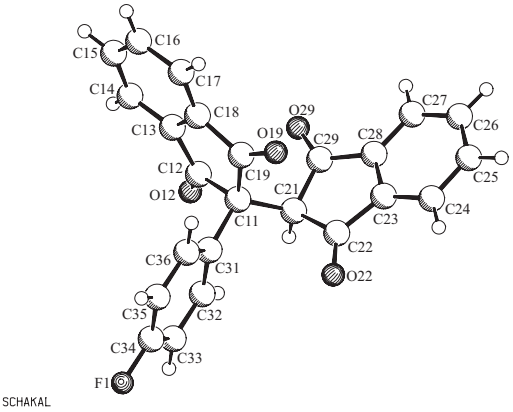


Fig. 1 X-ray crystal structure of **3b** with atom numbering scheme.

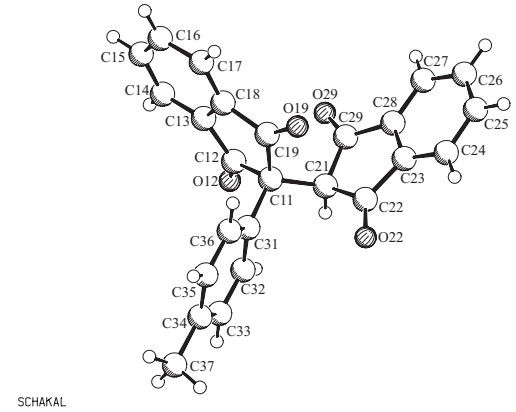
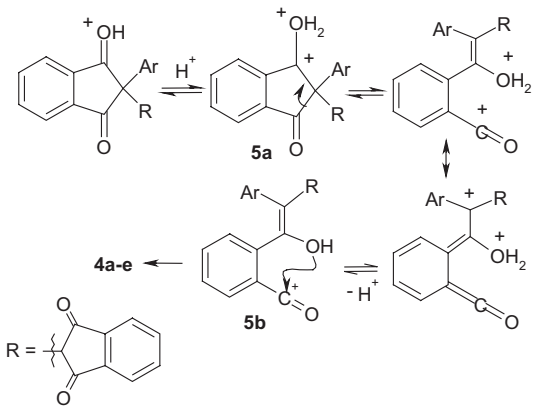


Fig. 2 X-ray crystal structure of **3f** with atom numbering scheme.

When arenes are stirred with **1** in triflic acid for a long period, totally different products are formed. The products are identified as isobenzofuranone derivatives **4a–e** (Table 1, Scheme 1). The adducts **3a–e** also give **4a–e** upon stirring in triflic acid. ^{1}H and ^{13}C NMR spectra of these adducts indicate an unsymmetrical structure. In the formation of **4**, three types of regioselectivity are observed. Firstly, the electrophilic attack occurs exclusively to the *para* position of the halobenzenes. Secondly, only the C-2 arylated 1,3-indanedionyl moiety takes part in the rearrangement to form the isobenzofuranone ring. Thirdly, the exocyclic 1,3-indanedionyl group in **4** is always in *trans* disposition with respect to the benzene ring of isobenzofuranone. As a result, selectively only one geometrical isomer is formed. These complex structural features of **4** are confirmed by the X-ray crystal structure of **4b** (Fig. 3).[10] In general, the rearrangement is found to be facile for compounds with electron-withdrawing substituents such as fluoro- and chlorobenzene (Table 1). Whereas for benzene and weakly electron-withdrawing arenes, such as bromo- and iodo-benzene the rearrangements are comparatively less facile (Table 1). In the case of electron-donating toluene the rearranged product of type **4** was not formed at all even after 3 days of stirring in triflic acid. Only the arylated adduct **3f** was isolated. In the formation of **4**, a dicationic intermediate **5a** may be formed which then undergoes ring-opening to spread out the accumulated positive charge on the carbonyl group (Scheme 2).[2] Subsequently a ring-closure produces **4**. Note that only the C-2 arylated 1,3-indanedionyl moiety of **3** participates in the rearrangement, because of the stability of intermediate **5b**.



Scheme 2

The adducts **3a–f** formed in superacid medium possess two 1,3-dicarbonyl moieties. Therefore nucleophilic attack on a C=O may facilitate the breaking of C_1-C_2 or $C_{1'}$-$C_{2'}$ bonds. Interestingly simple stirring of **3a–f** in hydrazine hydrate (99%) produces 4-[α-aryl-α-1,3-indanedionylmethyl]-1-(2*H*) phthalazinones **6a–f** in good yields (Scheme 3, Table 2). A set of adducts **3g–j** derived from the condensation of **1** with activated arenes such as anisole, veratrole, *o*-cresol and thymol,[1] also produces phthalazinones **6g–j** on treatment with hydrazine hydrate (Scheme 3). The structure of **6** was determined by ^{1}H and ^{13}C NMR spectroscopic analysis. In the ^{1}H NMR two characteristic doublets corresponding to two vicinal aliphatic protons in the side chain of **6** are observed, *e.g.* **6a**: 5.54 (d, J = 3.8 Hz, 1H), 3.58 (d, J = 3.8 Hz, 1H). Interestingly rearranged products **4** also give **6** on stirring in hydrazine hydrate (Scheme 3). The crystal structure of **6j** is presented in Fig. 4.[10]

When adducts **3** are refluxed in hydrazine hydrate (99%) more complex phthalazinones such as 1-aryl-1,2-di[3,4-dihydro-4-oxophthalazin-1-yl]ethanes **7** are formed

Table 2 Formation of phthalazinones **6a–j** from **3a–j**

Substrates	Products	Time/h	Yield/%	M.p./°C
3a	**6a**	3.0	71	256–257
3b	**6b**	3.0	73	273–274
3c	**6c**	2.5	74	251–252
3d	**6d**	2.0	70	225–226
3e	**6e**	2.0	68	278–279
3f	**6f**	2.5	75	284–285
3g	**6g**	2.0	76	265–266
3h	**6h**	2.5	75	247–248
3i	**6i**	2.0	72	285–286
3j	**6j**	3.0	72	288–289

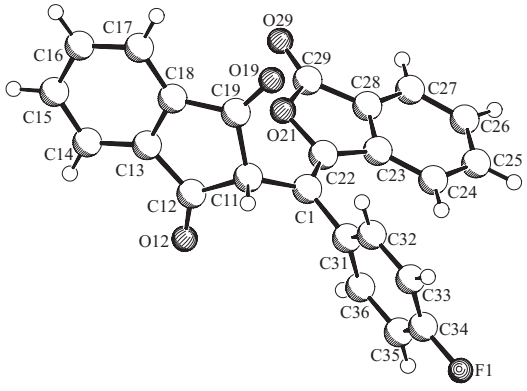
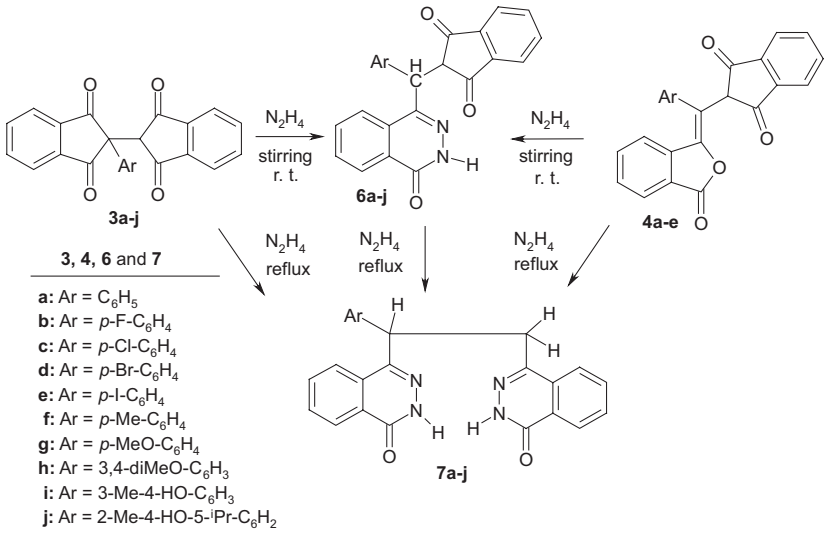


Fig. 3 X-ray crystal structure of **4b** with atom numbering scheme.



Scheme 3

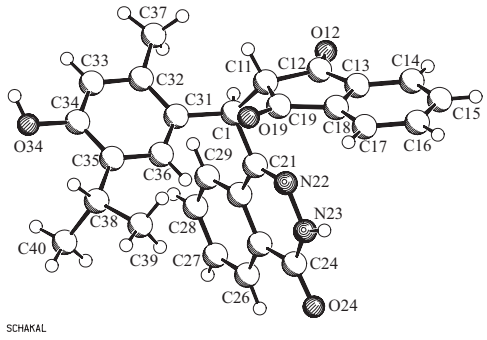
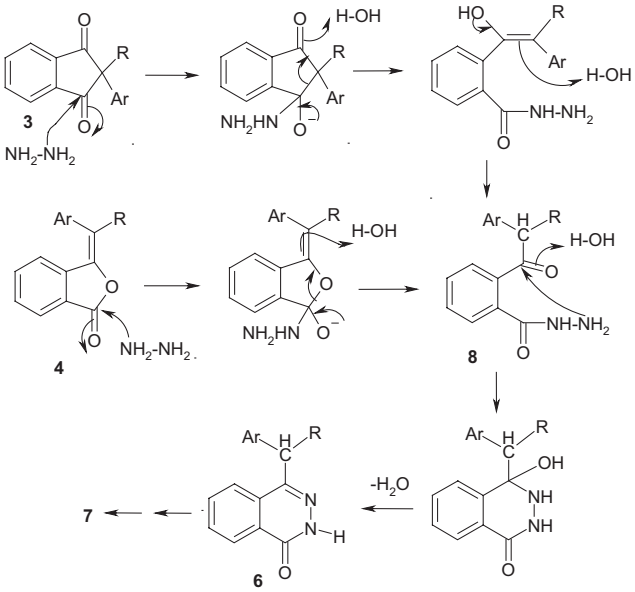


Fig 4 X-ray crystal structure of **6j** with atom numbering scheme

(Scheme 3, Table 3). They are confirmed by ^{1}H and ^{13}C NMR studies in DMSO-d_6. Due to the presence of the chiral centre at C_1 the methylene protons at C_2 become magnetically non-equivalent producing an ABX type of system. As a result two doublet of doublets (*dd*) proton signals are observed at δ 4.10 (dd, J = 16.0, 9.1 Hz) and 3.39 (dd, J = 16.0, 5.6 Hz) for methylene protons in the case of **7a**. The proton at C_1 should then appear as a double doublet (dd) with coupling constants of 5.6 and 9.1. Actually it has appeared as a quartet (q) at δ 5.37 because one coupling constant is almost double the value of the other. This is a common feature observed in all compounds **7**. The ^{1}H NMR spectrum of **7a** also shows two characteristic singlets at δ 12.59 and 12.32 for two amide protons. All the compounds **7** have similar spectroscopic (^{1}H and ^{13}C NMR) characteristics to those of **7a**. The present method provides a general and efficient route to complex 4-substituted phthalazinones which are otherwise difficult to prepare.

Table 3 Formation of phthalazinones **7a–j** from **3a–j**

Substrates	Products	Time/h	Yield/%	M.p./°C
3a	**7a**	9.0	60	354–56
3b	**7b**	9.0	62	303–04
3c	**7c**	8.0	60	334–35
3d	**7d**	8.0	58	350–52
3e	**7e**	9.0	55	356–58
3f	**7f**	8.0	60	332–34
3g	**7g**	9.0	65	325–26
3h	**7h**	9.0	62	318–20
3i	**7i**	9.0	62	336–38
3j	**7j**	9.0	55	303–04



Scheme 4

A proposed mechanism for the formation of **6** from **3** is depicted in Scheme 4. The nucleophilic attack of hydrazine at either of the carbonyl groups at C_1 or C_3 of **3** produces the open chain hydrazide **8**, which undergoes a subsequent intramolecular nucleophilic attack to the other C=O group, followed by dehydration to produce **6**. The same series of reactions are repeated by the remaining 1,3-indanedionyl group of **6** to give the final products **7**. Isobenzofuranones **4** also react with hydrazine hydrate in a similar way to **3** (Scheme 4). Under the heating conditions none of the intermediates, such as **8**, **6**, *etc*., could be isolated.

In summary, we have shown that in a superacid medium 2-hydroxy-2,2'-biindan-1,1',3,3'-tetrone **1** condenses with moderately activated and deactivated aromatics to produce arylated adducts, 2-aryl-2,2'-biindan-1,1',3,3'-tetrones **3**. Prolonged stirring of the same reaction mixture affords rearranged products 3-(aryl-1,3-indanedionylmethylene)isobenzofuranones **4**. Both the arylated adducts **3** and rearranged products **4** can also generate 4-substituted phthalazinones such as 4-[α-aryl-α-1,3-indanedionylmethyl]-1-(2*H*)phthalazinones **6** and 1-aryl-1,2-di[3,4-dihydro-4-oxophthalazin-1-yl]ethanes **7** by condensation with hydrazine hydrate.

Experimental

Melting points were determined in open capillary tubes and were uncorrected. IR spectra were examined in KBr disc on a Perkin Elmer-782 spectrophotometer. Proton magnetic resonance spectra (^{1}H NMR) and carbon magnetic resonance spectra (^{13}C NMR) were recorded on a Bruker Avance 300 (300 MHz) or a Bruker DRX-500 (500 MHz) spectrometer in the solvents indicated. Elemental analyses were performed on a Perkin-Elmer 240 C analyser. Triflic acid (CF_3SO_3H) was purchased from Aldrich and used as received.

General procedure for preparation of 2-aryl-2,2'-biindan-1,1',3,3'-tetrones **(3a–f)**

To a solution of **1** (0.43 g, 1.4 mmol) in triflic acid (2 ml), 1 ml of the arene was added (Table 1). The mixture was stirred at room temperature for 1–2 h under a dry atmosphere and then poured over crushed ice. The products were extracted with $CHCl_3$. The combined organic layers were washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The resulting products were purified by silica-gel column chromatography using ethyl acetate/petroleum ether as eluent. The solid products were further purified by crystallisation from $CHCl_3$/petroleum ether.

2-Phenyl-2,2´-biindan-1,1',3,3'-tetrone **(3a)**: Colourless crystals; m.p. 238–239°C. IR (KBr): 1710, 1591, 1265, 761 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.02–7.82 (m, 8 H), 7.49–7.37 (m, 5 H), 4.32 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.9 (2C), 196.5 (2C), 142.0 (2C), 141.5 (2C), 136.0 (2C), 135.7 (2C), 132.9, 128.8 (2C), 128.3, 127.6 (2C), 124.0 (2C), 123.2 (2C), 63.5, 55.9. Anal. Calcd for $C_{24}H_{14}O_4$: C, 78.68; H, 3.85. Found: C, 78.8; H, 4.0%.

2-(4-Fluorophenyl)-2,2'-biindan-1,1',3,3'-tetrone **(3b):** Colourless crystals; m.p. 191–192°C. IR (KBr): 1707, 1590, 1508, 1261, 767 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.99–7.98 (m, 2 H), 7.89–7.80 (m, 6 H), 7.45–7.42 (m, 2 H), 7.08–7.03 (m, 2 H,), 4.24 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.8 (2C), 196.5 (2C), 142.0 (2C), 141.4 (2C), 136.1 (2C), 135.8 (2C), 129.5, 129.4, 124.1 (2C), 123.3 (2C), 116.0 (2C), 115.7 (2C), 62.6, 55.9. Anal. Calcd for $C_{24}H_{13}FO_4$: C, 75.00; H, 3.41. Found: C, 75.1; H, 3.55%.

2-(4-Chlorophenyl)-2,2'-biindan-1,1',3,3'-tetrone **(3c):** Colourless crystals; m.p. 202–203°C. IR (KBr): 1707, 1587, 1260, 749 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.02–7.98 (m, 2 H), 7.92–7.82 (m, 6 H), 7.42 (d, *J* = 9.0 Hz, 2 H), 7.35 (d, *J* = 9.0 Hz, 2 H), 4.26 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.6 (2C), 196.3 (2C), 141.9 (2C), 141.4 (2C), 136.2 (2C), 135.8 (2C), 134.7, 131.3, 129.1 (2C), 129.0 (2C), 124.1 (2C), 123.3 (2C), 62.6, 55.9. Anal. Calcd for $C_{24}H_{13}ClO_4$: C, 71.91; H, 3.27. Found: C, 72.0; H, 3.4%.

2-(4-Bromophenyl)-2,2'-biindan-1,1',3,3'-tetrone **(3d):** Colourless crystals; m.p. 189–190°C. IR (KBr): 1707, 1586, 1259, 748 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.03–7.97 (m, 2 H), 7.91–7.80 (m, 6 H,), 7.50 (d, *J* = 9.0 Hz, 2 H), 7.35 (d, *J* = 9.0 Hz, 2 H), 4.26 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.6 (2C), 196.3 (2C), 141.9 (2C), 141.3 (2C), 136.2 (2C), 135.8 (2C), 132.0 (2C), 131.9, 129.2 (2C), 124.0 (2C), 123.3 (2C), 122.9, 62.7, 55.8. Anal. Calcd for $C_{24}H_{13}BrO_4$: C, 64.74; H, 2.94. Found: C, 64.85; H, 3.1%.

2-(4-Iodophenyl)-2,2'-biindan-1,1',3,3'-tetrone **(3e):** Colourless crystals; m.p. 205–206°C. IR (KBr): 1702, 1587, 1261, 753 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.99–7.95 (m, 2 H), 7.89–7.77 (m, 6 H), 7.66 (d, *J* = 8.7 Hz, 2 H), 7.17 (d, *J* = 8.7 Hz, 2 H), 4.21 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.2 (2C), 196.0 (2C), 141.6 (2C), 141.0 (2C), 137.6 (2C), 135.8 (2C), 135.5 (2C), 132.3, 129.1 (2C), 123.7 (2C), 123.0 (2C), 94.4, 62.5, 55.4. Anal. Calcd for $C_{24}H_{13}IO_4$: C, 58.56; H, 2.66. Found: C, 58.7, H 2.8%.

2-(4-Methylphenyl)-2,2'-biindan-1,1',3,3'-tetrone **(3f):** Colourless crystals; m.p. 230–231˚C. IR (KBr): 1707, 1587, 1260, 767 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.99–7.96 (m, 2 H,), 7.89–7.79 (m, 6 H), 7.33 (d, *J* = 9.0 Hz, 2 H), 7.18 (d, *J* = 9.0 Hz, 2 H), 4.27 (s, 1 H), 2.33 (s, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 198.4 (2C), 197.1 (2C), 142.5 (2C), 141.9 (2C), 138.7, 136.3 (2C), 136.1 (2C), 130.2, 130.1 (2C), 127.9 (2C), 124.4 (2C), 123.7 (2C), 63.8, 56.2, 21.5. Anal. Calcd for $C_{25}H_{16}O_4$: C, 78.94; H, 4.24. Found: C, 79.05; H, 4.4%.

General procedure for preparation of 3-(aryl-1,3-indanedionyl-methylene)-isobenzofuranones **(4a–e)**

4a–e were prepared following a similar procedure to that of **3a–f**, except the reaction mixture was stirred for 12–24 h instead of 1–2 h (Table 1).

3-(Phenyl-1,3-indanedionylmethylene)isobenzofuranone **(4a):** Light yellow crystals; m.p. 266–267°C. IR (KBr): 1788, 1703, 1588, 1281, 1217, 989, 761 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.02–7.98 (m, 2 H), 7.90–7.83 (m, 3 H), 7.50–7.34 (m, 7 H), 6.45 (d, *J* = 7.8 Hz, 1 H), 4.86 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 196.9 (2C), 165.8, 142.3 (2C), 137.7, 135.8 (2C), 135.0, 134.1, 130.0, 129.7 (2C), 129.2 (2C), 128.9, 125.7, 125.3, 123.6 (2C), 123.3, 116.6, 59.8. Anal. Calcd for $C_{24}H_{14}O_4$: C, 78.68; H, 3.85. Found: C, 78.8; H, 4.0%.

3-(4-Fluorophenyl-1,3-indanedionylmethylene)isobenzo-furanone **(4b):** Yellow crystals; m.p. 239–240°C. IR (KBr): 1788, 1707, 1592, 1262, 1223, 1009, 972, 764 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.99–7.96 (m, 2 H), 7.89 (d, *J* = 7.7 Hz, 1 H), 7.86–7.83 (m, 2 H), 7.48 (t, *J* = 7.6 Hz, 1 H), 7.39-–7.36 (m, 3 H), 7.08 (t, *J* = 8.6 Hz, 2 H), 6.44 (d, *J* = 7.9 Hz, 1 H), 4.85 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.8 (2C), 165.6, 147.1, 142.2 (2C), 137.5, 135.9 (2C), 134.2, 131.8, 131.7, 130.2, 125.7, 125.5, 123.6 (2C), 123.1, 116.5 (2C), 116.2 (2C), 115.4, 59.8. Anal. Calcd for $C_{24}H_{13}FO_4$: C, 75.00; H, 3.41. Found: C, 75.1; H, 3.6%.

3-(4-Chlorophenyl-1,3-indanedionylmethylene)isobenzofuranone **(4c):** Yellow crystals; m.p. 210–211°C. IR (KBr): 1788, 1705, 1589, 1261, 1007, 971, 764 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.00–7.96 (m, 2 H), 7.90–7.81 (m, 3 H), 7.52–7.34 (m, 6 H,), 6.52 (d, *J* = 9.0 Hz, 1 H), 4.84 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 196.7 (2C), 165.6, 147.1, 142.2 (2C), 137.5, 135.9 (2C), 135.1, 134.3, 133.4, 131.2 (2C), 130.3, 129.6 (2C), 125.7, 125.5, 123.6 (2C), 123.2, 115.2, 59.7. Anal. Calcd for $C_{24}H_{13}ClO_4$: C, 71.91; H, 3.27. Found: C, 72.05; H, 3.4%.

3-(4-Bromophenyl-1,3-indanedionylmethylene)isobenzofuranone **(4d):** Light yellow crystals; m.p. 209–210°C. IR (KBr): 1788, 1705, 1586, 1260, 1005, 970, 761 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.99–7.95 (m, 2 H), 7.89–7.83 (m, 3 H), 7.52 (d, *J* = 9.0 Hz, 2 H), 7.49–7.39 (m, 2 H), 7.28 (d, *J* = 9.0 Hz, 2 H), 6.52 (d, *J* = 9.0 Hz, 1 H), 4.83 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 196.7 (2C), 165.6, 147.0, 142.2 (2C), 137.5, 136.0 (2C), 134.3, 134.0, 132.5 (2C), 131.5 (2C), 130.3, 125.7, 125.6, 123.7 (2C), 123.4, 123.2, 115.2, 59.7. Anal. Calcd for $C_{24}H_{13}BrO_4$: C, 64.74; H, 2.94. Found: C, 64.9; H, 3.1%.

3-(4-Iodophenyl-1,3-indanedionylmethylene)isobenzofuranone **(4e):** Light yellow crystals; m.p. 223–224°C. IR (KBr): 1788, 1711, 1590, 1276, 1105, 765 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.22–8.15 (m, 2 H), 7.97–7.83 (m, 6 H), 7.75 (d, *J* = 8.7 Hz, 2 H), 7.31 (d, *J* = 8.4 Hz, 2 H), 4.65 (s, 1 H). Anal. Calcd for $C_{24}H_{13}IO_4$: C, 58.56; H, 2.66. Found: C, 58.6; H, 2.8%.

General procedure for preparation of 4-[α-aryl-α-1,3-indanedionylmethyl]-1-(2H)phthalazinones **(6a–j):** The appropriate substrate **3a–j** (1.4 mmol) was added to hydrazine hydrate (10 ml, 99%) and the mixture was stirred at room temperature for the time indicated in Table 2. Then it was acidified with HCl (6 M) to pH 6. The solid product separated was filtered and washed thoroughly with water. The resulting solids were purified by crystallisation from acetone.

4-[α-Phenyl-α-1,3-indanedionylmethyl]-1-(2H)phthalazinone **(6a):** Colourless crystals; m.p. 256–257°C. IR (KBr): 3385, 3186, 3059 (N–H), 1702, 1659 (C=O), 1255, 758 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.71 (s, N−H), 8.36–8.33 (m, 1 H,), 8.00–7.92 (m, 2 H), 7.88–7.78 (m, 2 H), 7.71–7.60 (m, 2 H), 7.52–7.50 (m, 1 H), 7.36–7.30 (m, 5 H), 5.54 (d, *J* = 3.8 Hz, 1 H), 3.58 (d, *J* = 3.8 Hz, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 199.0, 197.6, 159.7, 144.3, 143.0, 140.8, 138.7, 135.4, 134.7, 133.4, 131.4, 129.1 (2C), 129.0, 128.7 (2C), 128.2, 127.6, 126.9, 125.8, 123.1, 122.9, 56.5, 47.4. Anal. Calcd for $C_{24}H_{16}N_2O_3$: C, 75.78; H, 4.24; N, 7.37. Found: C, 75.9; H, 4.4; N, 7.3%.

4-[α-(4-Fluorophenyl)-α-1,3-indanedionylmethyl]-1-(2H)phthalazinone **(6b):** Off-white crystals; m.p. 273–274°C. IR (KBr): 3178, 3051 (N–H), 1706, 1656 (C=O), 1597, 1253, 752 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.53 (s, N−H), 8.37–8.35 (m, 1 H), 8.02–7.93 (m, 2 H), 7.90–7.80 (m, 2 H), 7.73–7.63 (m, 2 H), 7.50–7.48 (m, 1 H), 7.36–7.31 (m, 2 H), 7.08–7.03 (m, 2 H), 5.52 (d, *J* = 3.9 Hz, 1 H), 3.55 (d, *J* = 3.9 Hz, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.8, 197.7, 159.6, 144.1, 142.9, 140.9, 135.6, 134.8, 133.5, 131.6, 130.8, 130.7, 128.8, 128.3, 127.1, 125.7, 123.2, 123.0, 115.9 (2C), 115.6 (2C), 56.4, 46.6. Anal. Calcd for $C_{24}H_{15}FN_2O_3$: C, 72.36; H, 3.80; N, 7.03. Found: C, 72.5; H, 3.95; N, 7.1%.

4-[α-(4-Chlorophenyl)-α-1,3-indanedionylmethyl]-1-(2H)phthalazinone **(6c):** Off-white crystals; m.p. 251–252°C. IR (KBr): 3175, 3047 (N–H), 1707, 1656 (C=O), 1594, 1253, 753 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.53 (s, N−H), 8.38–8.35 (m, 1 H), 8.01–7.94 (m, 2 H), 7.91–7.82 (m, 2 H), 7.73–7.63 (m, 2 H), 7.48–7.46 (m, 1 H), 7.36–7.31 (m, 4 H), 5.50 (d, *J* = 3.8 Hz, 1 H), 3.55 (d, *J* = 3.8 Hz, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.7, 197.6, 159.7, 143.8, 142.9, 140.8, 137.2, 135.6, 134.9, 133.6, 133.5, 131.6, 130.5 (2C), 129.0 (2C), 128.8, 128.3, 127.1, 125.6, 123.2,

123.0, 56.3, 46.7. Anal. Calcd for $C_{24}H_{15}ClN_2O_3$: C, 69.48; H, 3.64; N, 6.75. Found: C, 69.6; H, 3.7; N, 6.65%.

4-[α-(4-Bromophenyl)-α-1,3-indanedionylmethyl]-1-(2H) phthalazinone **(6d):** Light yellow crystals; m.p. 225–226°C. IR (KBr): 3178, 3051 (N–H), 1708, 1657(C=O), 1594, 1254, 752 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 9.50 (s, N−H), 8.37–8.34 (m, 1 H), 8.01–7.95 (m, 2 H), 7.90–7.79 (m, 2 H), 7.73–7.63 (m, 2 H), 7.51–7.45 (m, 3 H), 7.27 (d, *J* = 9.0 Hz, 2 H), 5.49 (d, *J* = 3.8 Hz, 1 H), 3.55 (d, *J* = 3.8 Hz, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.6, 197.5, 159.6, 143.7, 142.9, 140.8, 137.7, 135.6, 134.9, 133.6, 131.9 (2C), 131.6, 130.8 (2C), 128.7, 128.3, 127.1, 125.6, 123.2, 123.0, 121.8, 56.2, 46.7. Anal. Calcd for $C_{24}H_{15}BrN_2O_3$: C, 62.76; H, 3.29; N, 6.10. Found: C, 62.8; H, 3.4; N, 6.2%.

4-[α-(4-Iodophenyl)-α-1,3-indanedionylmethyl]-1-(2H) phthalazinone **(6e):** Light yellow crystals; m.p. 278–279°C. IR (KBr): 3322 (N–H), 1710, 1669 (C=O), 1594, 1261, 750 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 9.68 (s, N−H), 8.36–8.33 (m, 1 H), 8.00–7.92 (m, 2 H), 7.89–7.78 (m, 2 H), 7.73–7.63 (m, 4 H), 7.48–7.45 (m, 1 H), 7.11 (d, *J* = 8.4 Hz, 2 H), 5.47 (d, *J* = 3.8 Hz, 1 H), 3.54 (d, *J* = 3.8 Hz, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.6, 197.5, 159.6, 143.7, 142.9, 140.8, 138.4, 137.9 (2C), 135.6, 134.8, 133.6, 131.6, 131.0 (2C), 128.7, 128.2, 127.1, 125.6, 123.2, 123.0, 93.4, 56.2, 46.8. Anal. Calcd for $C_{24}H_{15}IN_2O_3$: C, 56.94; H, 2.99; N, 5.53. Found: C, 57.1; H, 3.2; N, 5.7%.

4-[α-(4-Methylphenyl)-α-1,3-indanedionylmethyl]-1-(2H)phthalazinone **(6f):** Colourless crystals; m.p. 284–285°C. IR (KBr): 3245 (N–H), 1710, 1680 (C=O), 1594, 1257, 766 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 9.35 (s, N–H), 8.35–8.32 (m, 1 H), 7.99–7.91 (m, 2 H), 7.87–7.78 (m, 2 H), 7.68–7.59 (m, 2 H), 7.53–7.50 (m, 1 H), 7.22 (d, *J* = 8.0 Hz, 2 H), 7.17 (d, *J* = 8.0 Hz, 2 H), 5.49 (d, *J* = 3.9 Hz, 1 H), 3.54 (d, *J* = 3.9 Hz, 1 H), 2.33 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 199.1, 197.7, 159.6, 144.5, 143.0, 140.9, 137.4, 135.6, 135.5, 134.7, 133.5, 131.5, 129.5 (2C), 129.1, 128.9 (2C), 128.2, 126.9, 125.9, 123.1, 122.9, 56.6, 47.0, 21.1. Anal. Calcd for $C_{25}H_{18}N_2O_3$: C, 76.13; H, 4.60; N, 7.10. Found: C, 76.3; H, 4.7; N, 7.2%.

4-[α-(4-methoxyphenyl)-α-1,3-indanedionylmethyl]-1-(2H)phthalazinone(**6g):** Colourless crystals; m.p. 265–266°C. IR (KBr): 3233 (N-H), 1708, 1670 (C=O), 1595, 1507, 1245, 753 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 10.55 (s, N–H), 8.32 (d, *J* = 7.5 Hz, 1 H), 7.98 (d, *J* = 7.5 Hz, 1 H), 7.91 (d, *J* = 7.5 Hz, 1 H), 7.87–7.79 (m, 2 H,), 7.67–7.60 (m, 2 H), 7.51(d, *J* = 7.5 Hz, 1 H), 7.25 (d, *J* = 8.5 Hz, 2 H), 6.86 (d, *J* = 8.5 Hz, 2 H), 5.47 (d, *J* = 3.5 Hz, 1 H), 3.78 (s, 3 H), 3.55 (d, *J* = 3.5 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 199.3, 198.0, 160.2, 159.0, 143.8, 143.3, 141.1, 135.5, 134.8, 133.3, 131.3, 131.1, 130.4 (2C), 129.2, 128.6, 126.7, 125.9, 123.1, 123.0, 114.2 (2C), 56.8, 55.4, 46.7. Anal. Calcd for $C_{25}H_{18}N_2O_4$: C, 73.16; H, 4.42; N, 6.83. Found: C, 73.3; H, 4.5; N, 6.75%.

4-[α-(3,4-dimethoxyphenyl)-α-1,3-indanedionylmethyl]-1-(2H)-phthalazinone (**6h):** Light yellow crystals; m.p. 247–248°C. IR (KBr): 3210 (N–H), 1708, 1666 (C=O), 1596, 1514, 1250, 759 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 9.36 (s, N–H), 8.35-8.32 (m, 1 H), 8.01–7.80 (m, 4 H), 7.68–7.54 (m, 3 H), 6.91(d, *J* = 1.8 Hz, 1 H), 6.88–6.80 (m, 2 H), 5.45 (d, *J* = 3.6 Hz, 1 H), 3.86 (s, 3 H), 3.85 (s, 3 H), 3.55 (d, *J* = 3.6 Hz,1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 199.5, 199.0, 160.0, 149.5, 148.9, 145.0, 143.5, 141.3, 135.9, 135.2, 133.9, 131.9, 131.5, 129.5, 128.6, 127.3, 126.3, 123.5, 123.3, 122.0, 112.7, 111.6, 57.0, 56.4, 56.2, 47.6, Anal. Calcd for $C_{26}H_{20}N_2O_5$: C, 70.90; H, 4.58; N, 6.36. Found: C, 71.0; H, 4.5; N, 6.5%.

4-[α-(3-Methyl-4-hydroxyphenyl)-α-1,3-indanedionylmethyl]-1-(2H)-phthalazinone (**6i):** Colourless crystals; m.p. 285–286°C. IR (KBr): 3575, 3182(N–H), 1704, 1657(C=O), 1595, 1254, 751 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ = 12.17 (s, N–H), 9.18 (s, 1 H), 8.15–8.13 (m, 1 H), 7.92–7.63 (m, 7 H), 7.04 (br. s, 1 H), 6.85 (d, *J* = 8.2 Hz, 1 H), 6.63 (d, *J* = 8.2 Hz, 1 H), 5.33 (d, *J* = 4.2 Hz, 1 H), 3.86 (d, *J* = 4.2 Hz, 1 H), 2.03 (s, 3 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 200.6, 198.7, 160.0, 155.2, 144.6, 143.6, 141.4, 136.5, 135.7, 134.3, 132.3, 132.2, 130.1, 129.5, 128.7, 128.5, 126.8, 126.6, 124.3, 123.6, 123.3, 115.2, 57.1, 46.4, 17.1. Anal. Calcd for $C_{25}H_{18}N_2O_4$: C, 73.16; H, 4.42; N, 6.83. Found: C, 73.3; H, 4.3; N, 7.0%.

4-[α-(2-methyl-4-hydroxy-5-isopropylphenyl)-α-1,3-indanedionylmethyl]-1-(2H)-phthalazinone (**6j):** Light yellow crystals; m.p. 288–289°C. IR (KBr): 3378, 2957 (N–H), 1699, 1667 (C=O), 1598, 1250, 768 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ = 12.20 (s, N-H), 9.07 (s, 1 H), 8.13–8.10 (m, 1 H), 7.92–7.86 (m, 4 H), 7.71–7.66 (m, 2 H), 7.28–7.25 (m, 1 H), 6.63 (s, 1 H), 6.55 (s, 1 H), 5.35 (d, *J* = 3.7 Hz, 1 H), 3.79 (d, *J* = 3.7 Hz, 1 H), 2.98–2.91 (m, 1 H), 2.44 (s, 3 H), 1.00 (d, *J* = 6.8 Hz, 3 H), 0.67 (d, *J* = 6.8 Hz, 3 H). Anal. Calcd for $C_{28}H_{24}N_2O_4$: C, 74.32; H, 5.35; N, 6.19. Found: C, 74.4; H, 5.5; N, 6.3%.

General procedure for preparation of 1-aryl-1,2-di[3,4-dihydro-4-oxophthalazin-1-yl]ethanes **(7a–j):** The appropriate intermediate **3a–j** (1.4 mmol) was added to hydrazine hydrate (10 ml, 99%) and the mixture was heated in a boiling water-bath for the time indicated in Table 3. During heating some solid product was precipitated. The cooled reaction mixture was acidified with HCl (6 M) to pH 6. The solid product separated was filtered and washed thoroughly with water. The resulting solids were purified by crystallisation from acetone.

1-Phenyl-1,2-di[3,4-dihydro-4-oxophthalazin-1-yl]ethane **(7a):** Colourless crystals; m.p. 354–356°C. IR (KBr): 3169, 3033, 2900 (N–H), 1650 (C=O), 1348, 781 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ = 12.59 (s, N–H), 12.32 (s, N–H), 8.24 (d, *J* = 7.4 Hz, 2 H), 8.07–8.00 (m, 2 H), 7.92–7.74 (m, 4 H), 7.39 (d, *J* = 7.5 Hz, 2 H), 7.27 (t, *J* = 7.3 Hz, 2 H), 7.17 (t, *J* = 7.0 Hz, 1 H), 5.37 (*apparent* q, 1 H), 4.10 (dd, *J* = 16.0, 9.1 Hz, 1 H), 3.39 (dd, *J* = 16.0, 5.6 Hz, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 159.7, 159.6, 146.5, 144.3, 142.9, 134.0, 133.9, 131.8, 131.7, 130.0, 129.7, 129.2 (2C), 128.4 (2C), 127.8, 127.3, 126.5, 126.3, 125.7, 125.5, 43.5, 36.5. Anal. Calcd for $C_{24}H_{18}N_4O_2$. C, 73.08; H, 4.60; N, 14.21. Found: C, 73.2; H, 4.7; N, 14.3%.

1-(4-Fluorophenyl)-1,2-di[3,4-dihydro-4-oxophthalazin-1-yl]ethane **(7b):** Colourless crystals; m.p. 303–304°C. IR (KBr): 3172, 3014, 2899(N–H), 1653 (C=O), 1504, 1349, 780 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ = 12.59 (s, N–H), 12.32 (s, N–H), 8.24 (d, *J* = 7.4 Hz, 2 H), 8.08–8.00 (m, 2 H), 7.93–7.76 (m, 4 H), 7.45–7.40 (m, 2 H), 7.09 (t, *J* = 8.6 Hz, 2 H), 5.38 (*apparent* q, 1 H), 4.07 (dd, *J* = 15.9, 9.0 Hz, 1 H), 3.36 (dd, *J* = 15.9, 5.7 Hz, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 159.3, 159.2, 146.1, 143.9, 138.6, 133.6, 131.5, 131.4, 130.0, 129.9, 129.6, 129.2, 128.0, 127.4, 126.1, 126.0, 125.3, 125.1, 115.6 (2C), 115.4 (2C), 42.3, 36.2. Anal. Calcd for $C_{24}H_{17}FN_4O_2$: C, 69.90; H, 4.15; N, 13.58. Found: C, 70.0; H, 4.3; N, 13.7%.

1-(4-Chlorophenyl)-1,2-di[3,4-dihydro-4-oxophthalazin-1-yl]ethane **(7c):** Colourless crystals; m.p. 334–335°C. IR (KBr): 3171, 3041, 2895 (N–H), 1657 (C=O), 1483, 1347, 787 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ = 12.62 (s, N–H), 12.33 (s, N–H), 8.24 (d, *J* = 6.7 Hz, 2 H), 8.08–7.99 (m, 2 H), 7.90–7.78 (m, 4 H), 7.41 (d, *J* = 7.5 Hz, 2 H), 7.33 (d, *J* = 7.5 Hz, 2 H), 5.38 (*apparent* q, 1 H), 4.07 (dd, *J* = 15.7, 8.5 Hz, 1 H), 3.38 (dd, *J* = 15.7, 5.8 Hz, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 159.7, 159.6, 146.2, 144.2, 141.9, 134.0, 133.9, 132.0, 131.9, 131.8, 130.3 (2C), 129.9, 129.6, 129.1 (2C), 128.4, 127.8, 126.5, 126.4, 125.6, 125.5, 42.8, 36.4. Anal. Calcd for $C_{24}H_{17}ClN_4O_2$: C, 67.20; H, 3.99; N, 13.07. Found; C, 67.3; H, 4.15; N, 13.2%.

1-(4-Bromophenyl)-1,2-di[3,4-dihydro-4-oxophthalazin-1-yl]ethane **(7d):** Colourless crystals; m.p. 350–352°C. IR (KBr): 3169, 3036, 2893 (N–H), 1657 (C=O), 1476, 1345, 784 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ = 12.62 (s, N–H), 12.33 (s, N–H), 8.24 (d, *J* = 7.6 Hz, 2 H), 8.07 (d, *J* = 7.6 Hz, 1 H), 8.00 (d, *J* = 7.5 Hz, 1 H), 7.93–7.76 (m, 4 H), 7.46 (d, *J* = 8.0 Hz, 2 H), 7.35 (d, *J* = 8.0 Hz, 2 H), 5.36 (*apparent* q, 1 H), 4.07 (dd, *J* = 15.9, 8.9 Hz, 1 H), 3.37 (dd, *J* = 15.9, 5.7 Hz, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 159.7, 159.6, 146.2, 144.1, 142.3, 134.0, 133.9, 132.0 (2C), 131.9, 131.8, 130.7 (2C), 129.9, 129.6, 128.4, 127.8, 126.5, 126.4, 125.6, 125.5, 120.5, 42.8, 36.3. Anal. Calcd for $C_{24}H_{17}BrN_4O_2$: C, 60.90; H, 3.62; N, 11.84. Found: C, 61.05; H, 3.7; N, 12.0%.

1-(4-Iodophenyl)-1,2-di[3,4-dihydro-4-oxophthalazin-1-yl]ethane **(7e):** Light yellow crystals; m.p. 356–358°C. IR (KBr): 3168, 3036, 2892 (N–H), 1654 (C=O), 1474, 1345, 783 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ = 12.61 (s, N–H), 12.33 (s, N–H), 8.24 (d, *J* = 7.1 Hz, 2 H), 8.07 (d, *J* = 7.4 Hz, 1 H), 7.98 (d, *J* = 7.3 Hz, 1 H), 7.93–7.78 (m, 4 H), 7.63 (d, *J* = 7.5 Hz, 2 H), 7.20 (d, *J* = 7.5 Hz, 2 H), 5.33 (*apparent* q, 1 H), 4.06 (dd, *J* = 15.8, 8.4 Hz, 1 H), 3.38 (dd, *J* = 15.8, 5.7 Hz, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 159.7, 159.6, 146.1, 144.1, 142.7, 137.9 (2C), 134.0, 133.9, 131.9, 131.8, 130.8 (2C), 129.9, 129.6, 128.3, 127.8, 126.5, 126.4, 125.6, 125.5, 93.3, 42.9, 36.3. Anal. Calcd for $C_{24}H_{17}IN_4O_2$: C, 55.40; H, 3.29; N,10.77. Found: C, 55. 6; H, 3.4; N, 10.9%.

1-(4-Methylphenyl)-1,2-di[3,4-dihydro-4-oxophthalazin-1-yl]ethane **(7f):** Colourless crystals; m.p. 332–334°C. IR (KBr): 3170, 3034, 2896 (N–H), 1657 (C=O), 1345, 776 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ = 12.56 (s, N–H), 12.33 (s, N–H), 8.24 (d, *J* = 7.5 Hz, 2 H), 8.05 (d, *J* = 7.7 Hz, 1 H), 7.99 (d, *J* = 7.7 Hz, 1 H), 7.92–7.74 (m, 4 H), 7.25 (d, *J* = 7.6 Hz, 2 H), 7.07 (d, *J* = 7.6 Hz, 2 H), 5.31 (*apparent* q, 1 H), 4.07 (dd, *J* = 15.9, 8.9 Hz, 1 H), 3.35 (dd, *J* = 15.9, 5.7 Hz, 1 H), 2.20 (s, 3 H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 159.7, 159.6, 146.6, 144.4, 139.9, 136.3, 134.0, 133.9, 131.8, 131.7, 130.0, 129.8 (2C), 128.4, 128.2 (2C), 127.8, 126.5, 126.3,

125.7, 125.4, 43.1, 36.5, 21.0. Anal. Calcd for $C_{25}H_{20}N_4O_2$: C, 73.51; H, 4.93; N, 13.72. Found: C, 73.6; H, 5.0; N, 13.8%.

1-(4-Methoxyphenyl)-1,2-di[3,4-dihydro-4-oxophthalazin-1-yl]ethane **(7g):** Colourless prisms; m.p. 325–326°C. IR (KBr): 3176 (N–H), 1653 (C=O), 1087, 780 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ = 12.51 (s, N–H), 12.27 (s, N–H), 8.19 (d, *J* = 7.6 Hz, 2 H), 7.97 (t, *J* = 8.3 Hz, 2 H), 7.87–7.69 (m, 4 H), 7.23 (d, *J* = 8.6 Hz, 2 H), 6.77 (d, *J* = 8.6 Hz, 2 H), 5.25 (*apparent* q, 1 H), 4.01(dd, *J* = 16.0, 9.0 Hz, 1 H), 3.61 (s, 3 H), 3.31 (dd, *J* = 16.0, 5.7 Hz, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 159.4, 159.3, 158.2, 146.4, 144.1, 134.3, 133.5, 133.4, 131.3, 131.2, 129.6, 129.3, 128.9 (2C), 128.0, 127.4, 126.1, 126.0, 125.2, 125.0, 114.2 (2C), 55.1, 42.6, 36.2. Anal. Calcd for $C_{25}H_{20}N_4O_3$: C, 70.74; H, 4.75; N, 13.20. Found: C, 70.8; H, 4.7; N, 13.3%.

*1-(3,4-Dimethoxyphenyl)-1,2-di[3,4-dihydro-4-oxophthalazin-1-yl]ethane***(7h):** Colourless needles; m.p. 318–320°C. IR (KBr): 3165 (N–H), 1650 (C=O), 1511, 1259, 778 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ = 12.52 (s, N–H), 12.30 (s, N–H), 8.19 (d, *J* = 7.6 Hz, 2 H), 7.99 (t, *J* = 7.4 Hz, 2 H), 7.89–7.76 (m, 4 H), 6.97 (s, 1 H), 6.76–6.71 (m, 2 H), 5.24 (*apparent* q, 1 H), 4.02 (dd, *J* = 16.2, 9.0 Hz, 1 H), 3.63 (s, 3 H), 3.61 (s, 3 H), 3.34 (dd, *J* = 16.2, 5.4 Hz, 1 H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 159.4, 159.3, 149.0, 147.9, 146.3, 144.2, 134.9, 133.5, 133.3, 131.4, 131.2, 129.7, 129.4, 128.0, 127.4, 126.0, 125.9, 125.3, 125.0, 119.9, 112.4 (2C), 55.7 (2C), 42.9, 36.1. Anal. Calcd for $C_{26}H_{22}N_4O_4$: C, 68.71; H, 4.88; N, 12.33. Found: C, 68.8; H, 4.95; N, 12.4%.

1-(3-Methyl-4-hydroxyphenyl)-1,2-di[3,4-dihydro-4-oxophthalazin-1-yl]ethane **(7i):** Colourless needles; m.p. 336–338°C. IR (KBr): 3166 (N–H), 2922, 1656 (C=O), 1490, 1246, 777 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6): δ = 12.50 (s, N–H), 12.29 (s, N–H), 9.19 (s, –OH, 1 H), 8.23 (d, *J* = 7.6 Hz, 2 H), 8.03 (d, *J* = 8.0 Hz, 1 H), 7.98 (d, *J* = 8.0 Hz, 1 H), 7.89 (t, *J* = 7.3 Hz, 1 H), 7.82 (t, *J* = 7.5 Hz, 2 H), 7.76 (t, *J* = 7.5 Hz, 1 H), 7.04 (*br.* s, 1 H), 6.96 (d, *J* = 8.0 Hz, 1 H), 6.65 (d, *J* = 8.0 Hz, 1 H), 5.18 (*apparent* q, 1 H), 4.03 (dd, *J* = 16.0, 9.2 Hz, 1 H), 3.31 (dd, *J* = 16.0, 5.3 Hz, 1 H), 2.02 (s, 3 H). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 160.2, 160.1, 155.0, 147.3, 145.1, 134.4, 134.3, 133.3, 132.2, 132.1, 130.7, 130.4, 130.2, 128.7, 128.1, 127.0, 126.8, 126.7, 126.2, 125.9, 124.9, 115.6, 43.3, 37.1, 17.0. Anal. Calcd for $C_{25}H_{20}N_4O_3$: C, 70.74; H, 4.75; N, 13.20. Found: C, 70.85; H, 4.8; N, 13.3%.

1-(2-methyl-4-hydroxy-5-isopropylphenyl)-1,2-di[3,4-dihydro-4-oxophthalazin-1-yl]- ethane **(7j):** Colourless crystals; m.p. 303–304°C. IR (KBr): 3299, (N–H), 2905, 1659(C=O), 1499, 1414, 1347, 773 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ = 12.54 (s, N–H), 12.33 (s, N–H), 9.06 (s, –OH, 1 H), 8.23 (d, *J* = 7.1 Hz, 2 H), 8.01 (d, *J* = 7.5 Hz, 1 H), 7.86–7.73 (m, 4 H), 7.60 (d, *J* = 7.5 Hz, 1 H), 6.75 (s, 1 H), 6.55 (s, 1 H), 5.30 (*apparent* q, 1 H), 3.95 (dd, *J* = 15.9, 9.2 Hz, 1 H), 3.25 (dd, *J* = 15.9, 5.7 Hz, 1 H), 2.97 (m, 1 H), 2.25 (s, 3 H), 1.04 (d, *J* = 6.8 Hz, 3 H), 0.84 (d, *J* = 6.8 Hz, 3 H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 159.7, 159.6, 153.4, 146.9, 144.8, 134.0, 133.9, 133.2, 132.3, 131.8, 131.6, 131.0, 130.1, 129.8, 128.2, 127.7, 126.5, 126.3, 125.6, 125.2, 125.1, 117.6, 40.0, 35.5, 26.7, 23.1, 22.6, 19.1. Anal. Calcd for $C_{28}H_{26}N_4O_3$: C, 72.08; H, 5.62; N, 12.01. Found: C, 72.2; H, 5.7; N, 12.15%.

X-ray crystal structure analysis

3b: Formula $C_{24}H_{13}FO_4$, *M* = 384.34, light yellow crystal 0.30 × 0.15 × 0.10 mm, *a* = 18.362(1), *b* = 15.767(1), *c* = 12.996(1) Å, β = 100.40(1)°, *V* = 3700.7(4) $Å^3$, ρ_{calc} = 1.380 g cm^{-3}, μ = 1.01 cm^{-1}, empirical absorption correction (0.970 ≤ *T* ≤ 0.990), *Z* = 8, monoclinic, space group *C*2/c (No. 15), λ = 0.71073 Å, *T* = 198 K, ω and φ scans, 14764 reflections collected (±*h*, ±*k*, ±*l*), [(sinθ)/λ] = 0.66 $Å^{-1}$, 4411 independent (R_{int} = 0.059) and 2883 observed reflections [*I* ≥ 2 σ(*I*)], 262 refined parameters, *R* = 0.049, wR^2 = 0.135, max. residual electron density 0.24 (–0.20) e $Å^{-3}$, hydrogen atoms calculated and refined riding.

3f: Formula $C_{25}H_{16}O_4$, *M* = 380.38, colourless crystal 0.35 × 0.15 × 0.15 mm, *a* = 18.814(1), *b* = 16.151(1), *c* = 12.817(1) Å, β = 102.86(1)°, *V* = 3796.9(4) $Å^3$, ρ_{calc} = 1.331 g cm^{-3}, μ = 7.32 cm^{-1}, empirical absorption correction (0.784 ≤ *T* ≤ 0.898), *Z* = 8, monoclinic, space group *C*2/c (No. 15), λ = 1.54178 Å, *T* = 223 K, ω and φ scans, 14159 reflections collected (±*h*, ±*k*, ±*l*), [(sinθ)/λ] = 0.60 $Å^{-1}$, 3311 independent (R_{int} = 0.032) and 3114 observed reflections [*I* ≥ 2 σ(*I*)], 263 refined parameters, *R* = 0.040, wR^2 = 0.104, max. residual electron density 0.20 (–0.17) e $Å^{-3}$, hydrogen atoms calculated and refined riding.

4b: Formula $C_{24}H_{13}FO_4$, *M* = 384.34, yellow crystal 0.40 × 0.35 × 0.15 mm, *a* = 7.603(1), *b* = 10.584(1), *c* = 12.369(1) Å, α = 64.71(1), β = 84.66(1), γ = 83.42(1)°, *V* = 892.9(2) $Å^3$, ρ_{calc} = 1.429 g cm^{-3}, μ = 8.69 cm^{-1}, empirical absorption correction (0.723 ≤ *T* ≤ 0.881), *Z* = 2, triclinic, space group *P*1bar (No. 2), λ = 1.54178 Å, *T* = 223 K, ω and φ scans, 9277 reflections collected (±*h*, ±*k*, ±*l*), [(sinθ)/λ] = 0.60 $Å^{-1}$, 3098 independent(R_{int} = 0.029) and 2992 observed reflections [*I* ≥ 2 σ(*I*)], 262 refined parameters, *R* = 0.043, wR^2 = 0.116, max. residual electron density 0.20 (–0.32) e $Å^{-3}$, hydrogen atoms calculated and refined riding.

6j: Formula $C_{28}H_{23}N_2O_4$ * C_3H_6O, *M* = 510.57, light yellow crystal 0.15 × 0.10 × 0.05 mm, *a* = 8.236(1), *b* = 12.667(1), *c* = 13.204(2) Å, α = 100.94(1), β = 92.55(1), γ = 102.39(1)°, *V* = 1315.8(2) $Å^3$, ρ_{calc} = 1.289 g cm^{-3}, μ = 7.10 cm^{-1}, no absorption correction (0.901 ≤ *T* ≤ 0.965), *Z* = 2, triclinic, space group *P*1bar (No. 2), λ = 1.54178 Å, *T* = 223 K, ω and φ scans, 5978 reflections collected (±*h*, ±*k*, ±*l*), [(sinθ)/λ] = 0.57 $Å^{-1}$, 2444 independent (R_{int} = 0.112) and 1064 observed reflections [*I* ≥ 2 σ(*I*)], 352 refined parameters, *R* = 0.088, wR^2 = 0.202, max. residual electron density 0.31 (–0.30) e $Å^{-3}$, hydrogen atoms calculated and refined riding, due to the small and poorly diffracting crystal the analysis is of limited accuracy and was only done to prove the connectivity and conformation.

CCDC 281591 (**3b**), CCDC 281590 (**3f**), CCDC 281592 (**4b**) and CCDC 258440 (**6j**) contain the supplementary crystallographic data for this paper. They can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request.cif.

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