A catalyst-free and easy nucleophilic addition of certain isatins to sterically hindered 2,6-di-tert-butyl-4-methylene cyclohexa-2,5-dienone

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Abstract
Addition of substituted isatins to 2,6-di-tert-butyl-4-methylene cyclohexa-2,5-dienone, generated in situ from 3,5-di-tert-butyl-4-hydroxybenzyl acetate, to form 1-substituted hydroxybenzyl-isatins, is reported. On the basis of these isatins novel isatin-3-thiosemicarbazones as well as isoindigo derivatives bearing a 2,6-di-tert-butylphenol moiety were obtained. The structures of all novel compounds are confirmed by IR, 1H NMR and 13C NMR.

Keywords: Isatin, quinone methides, isoindigo, hydrazones, nucleophilic addition

Introduction
Isatin is a synthetically attractive substance due to its versatility in the chemistry of heterocycles.1-5 It is often used as a starting point in the synthesis of dyes and biologically active compounds.6-10 Isatin derivatives (Figure 1) also find applications in the field of solar energy,11-13 organic memory devices14 and organic field-effect transistors15,16

Nevertheless there are only a few works that deal with investigations of the addition reactions of isatin derivatives with multiple carbon-carbon bonds. Thus, an addition of isatin and some of its derivatives to the C=N bond of isocyanates and C=C bond of diphenylketene to form 1-carbamoylisatins and 1-diphenylacetylisatin respectively, have been described.17,18 The presence of an organocatalyst (triphenylphosphine (arsine), triethyl phosphite, DABCO, isocyanides) allows the addition of isatin to double carbon-carbon bonds of fumaric and acrylic esters.19-24 In all cases formation of a carbon-nitrogen bond is realized.
Results and Discussion

Herein we report the synthesis of novel isatin derivatives containing sterically hindered 2,6-di-tert-butylphenol fragment. This approach is based on the condensation reaction of substituted isatins 1a-d with 3,5-di-tert-butyl-4-hydroxybenzyl acetate 2 to give corresponding benzylisatins 3a-d with high yields (Scheme 1).

Scheme 1. Synthesis of novel sterically hindered benzylisatins 3a-d.

The reaction proceeds in dipolar aprotic solvents such as DMF or DMSO. These conditions allows in situ generation of the highly reactive \( p \)-quinone methide 4 which immediately undergoes addition of corresponding isatin 1a-d with formation of a carbon-nitrogen bond (Scheme 2). It should be noted here that the reaction takes place despite the hindrance due to the methyl group at the 7 position of the isatin heterocycle.
Scheme 2. *In situ* generation of 2,6-di-tert-butyl-4-methylene cyclohexa-2,5-dienone.

Next, on the basis of novel isatins 3a-d we succeeded in obtaining the corresponding isatin-3-thiosemicarbazides 7a-d and acylhydrazones 8a-d (Scheme 3).

Scheme 3. Novel isatin-3-thiosemicarbazones 7a-d and acylhydrazones 8a-d.

The structures of the novel compounds 7a-d and 8a-d were determined by spectroscopic methods (IR, $^1$H and $^{13}$C NMR spectroscopy) and by elemental analyses. The presence of an NH-
proton signal at 12-13 ppm in the $^1$H NMR spectra of compounds 7 and 8 points to the existence of these compounds as $Z_{C=N}$ – isomers with strong intramolecular N-H-O bond.\(^{26}\) (Figure 2)

![cis, Z and trans, Z-isomers of compounds 7a-d and 8a-d.](image)

**Figure 2.** Representation of cis,Z and trans,Z-isomers of compounds 7a-d and 8a-d.

A doubling of the C(O)CH$_2$, H-4 and N-H – proton signals in $^1$H NMR spectra of compounds 8a-d proves the presence of cis- and trans-forms regarding C(O)-N – fragment\(^{26}\) (Table 1). Similar doubling of NH, H-4, H-6 and NH$_2$ – signals in $^1$H NMR spectra also takes place for compound 7c.

**Table 1.** Selected signals of cis-C(O)-N and trans-C(O)-N – forms of $E_{C=N}$ – isomers in $^1$H NMR spectra of compounds 8a-d

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<th>Compd</th>
<th>C(O)CH$_2$, δ, ppm</th>
<th>H-4, δ, ppm</th>
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In a development of our investigations on the reactivity of 1,2-diketones\(^{27-30}\) towards trivalent phosphorus derivatives, isatins 3b-d were treated with tris(diethylamino)phosphine. The reaction proceeds in mild conditions and after the addition of the phosphorus reactant at -60 °C immediately turns dark. Then on spontaneous warming to room temperature the reaction mixture become successively brown, dark-violet, dark-red and finally purple-colored, followed by precipitation of compounds 9b-d (Scheme 4).
Scheme 4. Synthesis of novel sterically-hindered isoindigo derivatives 9b-d.

The structures of novel compounds 9b-d were determined using IR, $^1$H and $^{13}$C NMR spectroscopy. Thus, for example, in compound 9d the most significant observation is the downfield shift of the H-4 signal from 7.51 ppm in the starting isatin 3d to 9.04 ppm in the corresponding isoindigo 9d. Probably this is due to the formation of intramolecular H-C=O bond. Additionally, as a result of deoxygenation and C=C bond formation the signal of the C-3 carbonyl carbon atom at 183.9 ppm shifts to a signal at 133.4 ppm.

Conclusions

In summary, a synthetic method for the preparation of novel highly functionalized benzylisatins was developed. It consists in nucleophilic addition of substituted isatins to an in situ generated highly reactive p-quinone methide. Furthermore, this approach allows access to various isatin-3-thiosemicarbazones and hydrazones as well as isoindigos which are interesting molecules for biological studies and radical-chain oxidation processes inhibitors.

Experimental Section

General. All melting points were measured with a Stuart digital SMP10 apparatus. Solvents were distilled and dried by standard literature procedures prior to use. Elemental analyses for C, H and N were performed using a CHNS-3 analyzer. IR spectra were measured with Bruker Vector-22 spectrometer as suspensions in Nujol. The $^1$H and $^{13}$C NMR spectra were recorded on a Bruker Avance-400 instrument (400 MHz for $^1$H and 100.6 MHz for $^{13}$C). Chemical shifts are
given in ppm (δ) relative to residual DMSO or CHCl₃ signals. Isatin derivatives 1a-d were prepared by known synthetic procedures.³¹-³³

**Preparation of N-substituted 3,5-di-tert-butyl-4-hydroxybenzylindoline-2,3-diones 3a-c.** A mixture of substituted isatin 1a-c (10 mmol), 3,5-di-tert-butyl-4-hydroxybenzylacetate 2 (1.73 g, 11 mmol) and triethylamine (a few drops) in absolute DMF (10 ml) was stirred under 70 °C for 5 h, and cooled to r.t. Resulted solution was treated with 10% aqueous NaCl (200 ml). Precipitate that formed was filtered off, washed with water and air-dried.

**5-Butyl-1-(3,5-di-tert-butyl-4-hydroxybenzyl)indoline-2,3-dione (3a).** Dark-orange solid, yield 83%, mp 106-107 °C, IR: (vmax, cm⁻¹): 3639 (OH), 1732 (C=O), 1619, 1595, 1488, 1436, 1336, 1285, 1236, 1179, 1162, 1124, 1026, 886. ¹H NMR (CDCl₃) δH 0.91 (t, 3JHH 8.5 Hz, 3H, CH₃), 1.32 (m, 2H, CH₂), 1.40 (s, 18H, t-Bu), 1.55 (m, 2H, CH₂), 2.56 (t, 2H, CH₂), 4.78 (s, 2H, CH₂), 5.21 (s, 1H, OH), 6.80 (d, 3JHH 8.1 Hz, 1H, H-7), 7.16 (s, 2H, H-10), 7.32 (dd, 3JHH 8.1 Hz, 4JHH 1.3 Hz, 1H, H-6), 7.42 (br s, 1H, H-4). ¹³C NMR (CDCl₃) δC 13.8, 22.1, 30.2, 30.9, 33.3, 34.7, 44.4, 110.7, 117.8, 124.8, 125.0, 125.5, 136.5, 138.1, 138.6, 149.2, 153.6, 158.4, 183.9. Anal. Calcd for C₂₇H₃₅NÖ₃ (421.26): C, 76.92; H, 8.37; N, 3.32%, Found: C, 76.86; H, 8.27; N, 3.18%.

**5-Bromo-1-(3,5-di-tert-butyl-4-hydroxybenzyl)indoline-2,3-dione (3b).** Orange solid, yield 92%, mp 178-180 °C, IR: (vmax, cm⁻¹): 3639 (OH), 1736 (C=O), 1604, 1331, 1237, 1178, 1159, 1127, 1033, 837. ¹H NMR (CDCl₃) δH 1.40 (s, 18H, t-Bu), 4.80 (s, 2H, CH₂), 5.24 (s, 1H, OH), 6.80 (d, 3JHH 8.4 Hz, 1H, H-7), 7.12 (s, 2H, H-10), 7.63 (dd, 3JHH 8.4 Hz, 4JHH 2.1 Hz, 1H, H-6), 7.70 (d, 4JHH 2.0 Hz, 1H, H-4). ¹³C NMR (CDCl₃) δC 30.2, 34.3, 44.5, 112.6, 116.5, 118.9, 124.7, 124.8, 128.1, 136.7, 140.3, 149.8, 153.8, 157.5, 182.4. Anal. Calcd for C₂₃H₁₆BrNÖ₃ (443.11): C, 62.17; H, 5.90; N, 3.15%, Found: C, 61.96; H, 5.77; N, 3.08%.

**5,7-Dibromo-1-(3,5-di-tert-butyl-4-hydroxybenzyl)indoline-2,3-dione (3c).** Bright-orange solid, yield 88%, mp 155-157 °C, IR: (vmax, cm⁻¹): 3619 (OH), 1740 (C=O), 1598, 1406, 1360, 1336, 1310, 1275, 1223, 1144, 885. ¹H NMR (CDCl₃) δH 1.40 (s, 18H, t-Bu), 5.20 (s, 1H, OH), 5.32 (s, 2H, CH₂), 7.21 (s, 2H, H-10), 7.68 (dd, 4JHH 2.0 Hz, 1H, H-6), 7.85 (d, 4JHH 2.0 Hz, 1H, H-4). ¹³C NMR (CDCl₃) δC 30.2, 34.3, 44.5, 112.6, 116.5, 118.9, 124.7, 124.8, 128.1, 136.7, 140.3, 149.8, 153.8, 157.5, 182.8. Anal. Calcd for C₂₃H₁₅Br₂NÖ₃ (521.02): C, 52.79; H, 4.82; N, 2.68%, Found: C, 52.66; H, 4.70; N, 2.51%.

**7-Methyl-1-(3,5-di-tert-butyl-4-hydroxybenzyl)indoline-2,3-dione (3d).** A solution of 7-methylisatin 1d (909 mg, 6 mmol) and 3,5-di-tert-butyl-4-hydroxybenzylacetate 2 (1.58 g, 6 mmol) in DMF (50 ml) was stirred under 70 °C for 5 h and additionally for 5 days at r.t. Then resulted solution was treated with 10% aqueous NaCl (200 ml) followed by extraction with ether (100 ml). Combined organic extracts was rotary evaporated to form 1.54 g (72%) of compound 3d as orange solid, mp 165-168 °C, IR: (vmax, cm⁻¹): 3643 (OH), 1742 (C=O), 1725 (C=O), 1602, 1437, 1365, 1345, 1248, 1212, 1171, 1155, 1051, 769. ¹H NMR (CDCl₃) δH 1.37 (s, 18H, t-Bu), 2.36 (s, 3H, CH₃), 5.08 (s, 2H, CH₂), 5.15 (s, 1H, OH), 7.00 (m, 1H, H-5), 7.01 (s, 2H, H-10), 7.28 (d, 3JHH 7.7 Hz, 1H, H-6), 7.51 (d, 3JHH 7.4 Hz, 1H, H-4). ¹³C NMR (CDCl₃) δC 18.8, 30.2,
General procedure for the synthesis of substituted 1-(3,5-di-tert-butyl-4-hydroxybenzyl)-indoline-2,3-dione 3-thiosemicarbazones 7a-d. A mixture of substituted isatin 3a-d (10 mmol), thiosemicarbazide hydrochloride 5 (75 mg, 12 mmol) and triethylamine (0.05 ml, 0.4 mmol) in ethanol (10 ml) was stirred at 80 °C for 6 h, then cooled to r.t. The precipitate was collected by filtration, washed with ethanol (25 ml) and air-dried to give 7.

5-Butyl-1-(3,5-di-tert-butyl-4-hydroxybenzyl)indoline-2,3-dione 3-thiosemicarbazone (7a). Yellow solid, yield 52%, mp 208 °C, IR: (ν_max cm⁻¹): 3577 (OH), 3413 (NH₂), 3245 (NH₂), 3157 (NH), 1685 (C=O), 1612 (C=N), 1446, 1310, 1240, 1191, 1140, 1127, 1027, 986, 850. ¹H NMR (CDCl₃) δ_H 0.92 (t, 3_J_HH 7.4 Hz, 3H, CH₃), 1.31-1.37 (m, 2H, CH₂), 1.40 (s, 1H, t-Bu), 1.55-1.61 (m, 2H, CH₂), 2.59 (br t, 2H, CH₂), 4.79 (s, 2H, CH₂), 5.20 (br s, 1H, OH), 6.55 (br s, 1H, NH₂), 6.82 (d, 1H, 3_J_HH 8.1 Hz, H-7), 7.14-7.15 (m, 2H, H-10, 1H, H-6), 7.39 (br s, 1H, H-4), 7.54 (br s, 1H, NH₂), 12.93 (s, 1H, NH-O). ¹³C NMR (CDCl₃) δ_C 13.9, 22.2, 30.2, 33.7, 34.3, 35.2, 43.9, 109.9, 119.4, 120.7, 124.8, 125.8, 131.5, 132.6, 136.4, 138.0, 141.6, 153.5, 161.1, 180.1. Anal. Calcd for C₂₉H₃₈N₄O₂S (594.27): C, 67.98; H, 7.74; N, 11.33%, Found: C, 67.71; H, 7.57; N, 11.19%.

5-Bromo-1-(3,5-di-tert-butyl-4-hydroxybenzyl)indoline-2,3-dione 3-thiosemicarbazone (7b). Yellow solid, yield 79%, mp 248-250 °C (dec.), IR: (ν_max cm⁻¹): 3619 (OH), 3412 (NH₂), 3248 (NH₂), 3172 (NH), 1682 (C=O), 1599 (C=N), 1461, 1354, 1328, 1239, 1161, 1145, 1124, 1058, 1031, 971, 817. ¹H NMR (DMSO-d₆) δ_H 1.33 (s, 18H, t-Bu), 4.84 (s, 2H, CH₂), 6.93 (s, 1H, OH), 7.12 (s, 2H, H-10), 7.14 (d, 3_J_HH 8.3 Hz 1H, H-7), 7.57 (dd, 3_J_HH 8.4 Hz, 4_J_HH 2.0 Hz, 1H, H-6), 7.95 (d, 4_J_HH 2.0 Hz 1H, H-4), 8.87 (s, 1H, NH₂), 9.15 (s, 1H, NH₂), 12.23 (s, 1H, NH-O). ¹³C NMR (DMSO-d₆) δ_C 30.2, 34.4, 43.0, 112.3, 114.8, 121.6, 123.3, 124.1, 126.4, 129.5, 133.0, 139.4, 141.8, 153.3, 160.3, 178.8. Anal. Calcd for C₂₉H₂₉BrN₄O₂S (516.12): C, 55.70; H, 5.65; N, 10.83%, Found: C, 55.53; H, 5.42; N, 10.68%.

5,7-Dibromo-1-(3,5-di-tert-butyl-4-hydroxybenzyl)indoline-2,3-dione 3-thiosemicarbazone (7c). Isomers ratio 3:1. Yellow solid, yield 96%, 220 mg, mp 240 °C (dec.), IR: (ν_max cm⁻¹): 3623 (OH), 3414 (NH₂), 3248 (NH₂), 3156 (NH₂), 1694 (C=O), 1603 (C=N), 1554, 1463, 1444, 1343, 1320, 1237, 1151, 1127, 1074, 1038, 976, 861, 786, 725. ¹H NMR (DMSO-d₆) δ_H (major isomer) 1.31 (s, 18H, t-Bu), 5.21 (s, 2H, CH₂), 6.90 (s, 1H, OH), 7.02 (s, 2H, H-10), 7.81 (d, 4_J_HH 1.8 Hz, 1H, H-4), 8.09 (d, 4_J_HH 2.0 Hz, 1H, H-6), 8.99 (s, 1H, NH₂), 9.24 (s, 1H, NH₂), 12.13 (s, 1H, NH-O); (minor isomer) 1.31 (s, 18H, t-Bu), 5.21 (s, 2H, CH₂), 6.90 (s, 1H, OH), 7.02 (s, 2H, H-10), 7.77 (d, 4_J_HH 1.8 Hz, 1H, H-4), 7.91 (d, 4_J_HH 1.6 Hz, 1H, H-6), 8.87 (s, 1H, NH₂), 9.16 (s, 1H, NH₂), 12.23 (s, 1H, NH-O). ¹³C NMR (DMSO-d₆) δ_C 30.2, 34.5, 43.8, 103.6, 115.3, 122.7, 123.1, 124.7, 127.5, 128.1, 136.9, 139.0, 139.2, 153.0, 161.1, 178.8. Anal. Calcd for C₂₉H₂₈Br₂N₂O₂S (594.03): C, 48.33; H, 4.73; N, 9.39%, Found: C, 48.15; H, 4.49; N, 9.18%.
7-Methyl-1-(3,5-di-tert-butyl-4-hydroxybenzyl)indoline-2,3-dione 3-thiosemicarbazone (7d). Yellow solid, yield 71%, mp 236 °C (dec.), IR: (v_{max}, cm^{-1}): 3631 (OH), 3396 (NH₂), 3291-3256 (NH₂), 3155 (NH), 1675 (C=O), 1604 (C=N), 1463, 1439, 1357, 1337, 1240, 1139, 1106, 1075, 1004, 869, 824, 799, 743, 704, 622. ¹H NMR (DMSO-d₆) δH 1.29 (s, 18H, t-Bu), 2.29 (s, 3H, CH₃), 5.08 (s, 2H, CH₂), 6.92 (s, 1H, OH), 6.93 (s, 2H, H-10), 7.05 (t, 3J_{HH} 7.6 Hz, 1H, H-5), 7.14 (d, 3J_{HH} 7.6 Hz, 1H, H-6), 7.66 (d, 3J_{HH} 7.6 Hz, 1H, H-4), 8.77 (s, 1H, NH₂), 9.09 (s, 1H, NH₂), 12.42 (s, 1H, NH-O). ¹³C NMR (DMSO-d₆) δC 17.8, 30.2, 34.4, 44.1, 118.8, 120.1, 121.0, 122.0, 123.1, 127.9, 130.6, 134.8, 139.6, 140.8, 152.9, 161.6, 178.7. Anal. Calcd for C_{25}H_{32}N_{4}O_{2}S (452.22): C, 66.34; H, 7.13; N, 12.38%. Found: C, 66.15; H, 6.98; N, 12.05%.

General procedure for the synthesis of substituted 3-(3,5-di-tert-butyl-4-hydroxyphenyl)-propionic acid [1-(3,5-di-tert-butyl-4-hydroxybenzyl)-2-oxo-1,2-dihydroindol-3-ylidene]hydrazides 8a-d. A mixture of substituted isatin 3a-d (10 mmol), 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionic acid hydrazide 6 (140 mg, 10 mmol) and trifluoroacetic acid (0.5 ml) in ethanol (10 ml) was stirred at 70 °C for 5 h, and cooled to r.t. The precipitate was filtered off, washed with ethanol (25 ml) and air-dried to give 8a-d. 3-(3,5-Di-tert-butyl-4-hydroxyphenyl)propionic acid [5-buty1-1-(3,5-di-tert-butyl-4-hydroxybenzyl)-2-oxo-1,2-dihydroindol-3-ylidene]hydrazide (8a). Isomers ratio 2.5:1. Yellow solid, yield 45%, mp 156-158 °C, IR: (v_{max}, cm^{-1}): 3643 (OH), 3210 (NH), 1692 (C=O), 1625 (C=N), 1611, 1466, 1435, 1349, 1319, 1248, 1212, 1172, 1154, 1133, 1044, 1021, 989, 865, 818, 802, 785, 739, 545. ¹H NMR (CDCl₃) δH (minor isomer) 0.94 (t, 3H, Me), 1.30-1.40 (m, 2H, CH₂), 1.42 (s, 18H, t-Bu), 1.47 (s, 18H, t-Bu), 1.55-1.63 (m, 2H, CH₂), 2.60 (t, 2H, CH₂Ar), 2.74 (br t, 2H, CH₂(C(O))), 3.00 (br t, 2H, ArCH₂CH₂C(O)), 4.81 (s, 2H, NCH₂Ar), 5.08 (s, 1H, OH), 5.20 (s, 1H, OH), 6.82 (d, 1H, 3J_{HH} 7.9 Hz, H-7), 7.05-7.19 (m, 5H, H-6, H-10, H-16), 7.70 (s,1H, H₄), 13.13 (s,1H, NH-O), δH (major isomer) 0.94 (t, 3H, Me), 1.30-1.40 (m, 2H, CH₂), 1.42 (s, 18H, t-Bu), 1.45 (s, 18H, t-Bu), 1.55-1.63 (m, 2H, CH₂), 2.60 (t, 2H, CH₂Ar), 3.00 (br t ,2H, ArCH₂CH₂C(O)), 3.16 (br t, 2H, CH₂C(O)), 4.81 (s, 2H, NCH₂Ar), 5.10 (s, 1H, OH), 5.20 (s, 1H, OH), 6.82 (d, 1H, 3J_{HH} 7.9 Hz, H-7), 7.05-7.19 (m, 5H, H-6, H-10, H-16), 7.44 (s, 1H, H-4), 12.59 (s, 1H, NH-O). ¹³C NMR (CDCl₃) δC 13.4, 21.8, 29.7, 29.9, 30.3, 33.4, 33.8, 33.9, 34.1, 34.8, 43.3, 109.1, 119.6, 120.0, 124.3, 124.6, 125.6, 130.3, 131.3, 132.7, 135.5, 135.8, 137.5, 140.6, 151.7, 153.0, 160.5, 175.2. Anal. Calcd for C_{44}H_{61}N_{4}O_{7} (695.47): C, 75.93; H, 8.83; N, 6.04%. Found: C, 75.75; H, 8.80; N, 5.85%.

3-(3,5-Di-tert-butyl-4-hydroxyphenyl)propionic acid [5-bromo-1-(3,5-di-tert-butyl-4-hydroxybenzyl)-2-oxo-1,2-dihydroindol-3-ylidene]hydrazide (8b). Isomers ratio 3.8:1. Yellow solid, yield 85%, mp 170 °C, IR: (v_{max}, cm^{-1}): 3647 (OH), 3615 (OH), 3213 (NH), 1686 (C=O), 1609 (C=N), 1589, 1463, 1436, 1376, 1352, 1318, 1235, 1161, 1121, 1043, 984, 807, 791, 725. ¹H NMR (CDCl₃) δH minor isomer 1.42 (s, 18H, t-Bu), 1.47 (s, 18H, t-Bu), 2.76 (br t, 2H, CH₂C(O)), 3.00 (br t, 2H, ArCH₂CH₂C(O)), 4.82 (s, 2H, NCH₂Ar), 5.10 (s, 1H, OH), 5.23 (s, 1H, OH), 6.80 (d, 1H, 3J_{HH} 8.2 Hz, H-7), 7.11 (s, 2H, H-10), 7.13 (s, 2H, H-16), 7.99 (s, 1H, H-4), 13.02 (s, 1H, NH-O), δH major isomer 1.42 (s, 18H, t-Bu), 1.47 (s, 18H, t-Bu), 3.14 (br t,
2H, CH₂C(O)), 3.00 (br t, 2H, ArCH₂CH₂C(O)), 4.82 (s, 2H, NCH₂Ar), 5.10 (s, 1H, OH), 5.23 (s, 1H, OH), 6.80 (d, 1H, 3JHH 8.2 Hz, H-7), 7.11 (s, 2H, H-10), 7.13 (s, 2H, H-16), 7.44 (s, 1H, H-4), 12.51 (s, 1H, NH-O), 13C NMR (CDCl₃) δC 29.7, 29.9, 30.2, 33.8, 33.9, 34.0, 43.4, 110.8, 115.4, 121.4, 123.0, 124.1, 124.5, 124.9, 130.9, 131.0, 132.7, 135.5, 136.0, 141.3, 151.7, 153.2, 160.0, 175.1. Anal. Calcd for C₄₀H₃₂BrN₃O₄ (717.31): C, 66.84; H, 7.29; N, 5.85%. Found: C, 66.65; H, 7.98; N, 5.62%.

3-(3,5-Di-tert-butyl-4-hydroxyphenyl)propionic acid [5,7-dibromo-1-(3,5-di-tert-butyl-4-hydroxybenzyl)-2-oxo-1,2-dihydroindol-3-ylidene]hydrazide (8c). Isomers ratio 3:1. Yellow solid, yield 83%, mp 218 °C, IR: (νmax, cm⁻¹): 3631 (OH), 3279 (NH), 1731 (C=O), 1686 (C=O), 1602 (C=N), 1553, 1460, 1358, 1329, 1269, 1233, 1121, 1081, 985, 873, 729. ¹H NMR (CDCl₃) δH minor isomer 1.39 (s, 18H, t-Bu), 1.44 (s, 18H, t-Bu), 2.71 (br s, 2H, CH₂C(O)), 3.00 (br t, 2H, ArCH₂CH₂C(O)), 5.08 (s, 1H, OH), 5.17 (s, 1H, OH), 5.31 (s, 2H, NCH₂Ar), 7.07 (s, 2H, H-10), 7.18 (s, 2H, H-16), 7.64 (s, 1H, H-4); 7.68 (s, 1H, H-6), 13.00 (s, trans-Z, 1H, NH O); δH major isomer 1.39 (s, 18H, t-Bu), 1.44 (s, 18H, t-Bu), 3.10 (br s, 2H, CH₂C(O)), 3.00 (br t, 2H, ArCH₂CH₂C(O)), 5.08 (s, 1H, OH), 5.17 (s, 1H, OH), 5.31 (s, 2H, NCH₂Ar), 7.07 (s, 2H, H-10), 7.18 (s, 2H, H-16), 7.64 (s, 1H, H-4); 7.69 (s, 1H, H-6), 12.44 (s, cis-Z, 1H, NH O). Due to the very low solubility of this compound in a wide range of organic solvents ¹³C NMR spectrum could not be recorded. Anal. Calcd for C₄₀H₃₁Br₂N₄O₄ (795.22): C, 60.23; H, 6.44; N, 5.27%. Found: C, 60.07; H, 6.28; N, 5.19%.

3-(3,5-Di-tert-butyl-4-hydroxyphenyl)propionic acid [7-methyl-1-(3,5-di-tert-butyl-4-hydroxybenzyl)-2-oxo-1,2-dihydroindol-3-ylidene]hydrazide (8d). Isomers ratio 2:5:1. Yellow solid, yield 71%, mp 218-220 °C, IR: (νmax, cm⁻¹): 3627 (OH), 3285 (NH), 1713 (C=O), 1679 (C=O), 1596 (C=N), 1456, 1436, 1374, 1360, 1325, 1256, 1234, 1177, 1146, 1119, 1092, 1029, 875, 798, 741, 509. ¹H NMR (CDCl₃) δH minor isomer 1.38 (s, 18H, t-Bu), 1.44 (s, trans-Z, 18H, t-Bu), 2.38 (s, 3H, Me), 2.73 (br t, 2H, CH₂C(O)), 3.01 (br t, 2H, ArCH₂CH₂C(O)), 5.08 (s, 1H, OH), 5.12 (s, 2H, NCH₂Ar), 5.16 (s, 1H, OH), 6.95-7.15 (m, 6H, H-5, H-6, H-10, H-16), 7.75 (d, trans-Z, 1H, 3JHH 7.3 Hz, H-4), 13.16 (s, trans-Z, 1H, NH-O); major isomer 1.38 (s, 18H, t-Bu), 1.47 (s, cis-Z, 18H, t-Bu), 2.40 (s, 3H, Me), 3.17 (br t, 2H, CH₂C(O)), 3.01 (br t, 2H, ArCH₂CH₂C(O)), 5.10 (s, 1H, OH), 5.12 (s, 2H, NCH₂Ar), 5.16 (s, 1H, OH), 6.95-7.15 (m, 6H, H-5, H-6, H-10, H-16), 7.51 (d, cis-Z, 1H, 3JHH 7.3 Hz, H-4), 12.58 (s, cis-Z, 1H, NH-O), ¹³C NMR (CDCl₃) δC 18.3, 29.7, 29.9, 30.1, 33.8, 33.9, 34.0, 44.3, 118.0, 120.3, 120.4, 122.3, 122.7, 124.5, 126.8, 131.2, 132.2, 134.4, 135.5, 135.9, 140.7, 151.7, 152.7, 161.4, 175.1. Anal. Calcd for C₄₄H₃₅N₅O₄ (653.42): C, 75.31; H, 8.48; N, 6.43%. Found: C, 75.09; H, 8.28; N, 6.29%.

5,5'-Dibromo-1,1'-(3,5-di-tert-butyl-4-hydroxybenzyl)-1H,1'H-[3,3'-biindolylidene-2,2'-dione (9b). Dark-cherry solid, yield 91%, 437 mg, mp > 300 °C, IR: (νmax, cm⁻¹): 3616 (OH), 1695 (C=O), 1605 (C=C), 1300, 1213, 1157, 1120, 801. ¹H NMR (CDCl₃) δH 1.32 (s, 18H, t-Bu), 4.90 (s, 2H, CH₂), 6.92 (br s, 1H, OH), 7.11 (d, 3JHH 8.6 Hz, 1H, H-7), 7.14 (s, 2H, H-10), 7.64 (dd, 3JHH 8.5 Hz, 4JHH 1.6 Hz, 1H, H-6), 9.36 (d, 4JHH 1.6 Hz, 1H, H-4). Anal. Calcd for C₄₆H₅₂Br₂N₂O₄ (854.23): C, 64.49; H, 6.12; N, 3.27%. Found: C, 64.28; H, 6.01; N, 3.18%. Due
to the very low solubility of this compound in a wide range of organic solvents ¹³C NMR spectrum could not be recorded.

5,5',7,7'-Tetrabromo-1,1'- (3,5-di-tert-butyl-4-hydroxybenzyl)-1H,1'H-[3,3']-biindolylidene-2,2'-dione (9c). Light-purple solid, yield 83%, 215 mg, mp > 300 °C, IR: (υ_max, cm⁻¹): 3438 (OH), 1700 (C=O), 1608 (C=C), 1550, 1333, 1214, 1149, 1109, 1023. ¹H NMR (DMSO-d₆) δ_H 1.40 (s, 18H, t-Bu), 5.15 (br s, 1H, OH), 5.41 (s, 2H, CH₂), 7.20 (s, 2H, H-10), 7.67 (d, 4_J_HH 1.8 Hz, 1H, H-6), 9.37 (d, 4_J_HH 1.8 Hz, 1H, H-4). ¹³C NMR (DMSO-d₆) δ_C 30.3, 34.4, 44.9, 102.5, 115.1, 124.3, 125.8, 127.2, 131.4, 133.1, 136.0, 140.5, 141.2, 153.2, 168.0. Anal. Calcd for C₄₆H₅₀Br₄N₂O₄ (1010.05): C, 54.46; H, 4.97; N, 2.76%. Found: C, 54.28; H, 4.91; N, 2.60%.

7,7'-Dimethyl-1,1'- (3,5-di-tert-butyl-4-hydroxybenzyl)-1H,1'H-[3,3']-biindolylidene-2,2'-dione (9d). Dark-cherry crystals, yield 85%, 478 mg, mp 125 °C, IR: (υ_max, cm⁻¹): 3460 (OH), 1691 (C=O), 1600 (C=C), 1377, 1235, 1209, 1187, 1160, 1117, 1023, 787. ¹H NMR (CDCl₃) δ_H 1.36 (s, 18H, t-Bu), 2.36 (s, 3H, CH₃), 5.18 (s, 2H, CH₂), 6.90 (t, 3_J_HH 7.8 Hz, 1H, H-5), 7.01 (s, 2H, H-10), 7.04 (d, 3_J_HH 7.4 Hz, 1H, H-6), 9.04 (d, 3_J_HH 7.8 Hz, 1H, H-4). ¹³C NMR (CDCl₃) δ_C 19.2, 30.2, 34.3, 45.5, 119.1, 122.0, 122.6, 125.9, 127.3, 128.0, 133.4, 136.2, 136.6, 142.9, 152.9, 169.1. Anal. Calcd for C₄₈H₅₈N₂O₄ (726.44): C, 79.30; H, 8.04; N, 3.85%. Found: C, 79.18; H, 7.95; N, 3.68%.

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