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Supplementary material

Detailed solvent, structural, quantum chemical study and antimicrobial activity of isatin Schiff base

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1. Introduction

Table S1. Solvent parameters [1,2] used in Kamlet–Taft equation.

Solvent	π^*	α	β
Methanol (MeOH)	0.60	0.66	0.98
Ethanol (EtOH)	0.54	0.75	0.86
2-Propanol (iPrOH)	0.48	0.84	0.76
2-Butanol (2-BuOH)	0.40	0.80	0.69
Cyclohexanol (ChO)	0.45	0.84	0.66
Benzyl alcohol (BzOH)	0.98	0.52	0.60
2-Methoxyethanol (2ME)	0.71	0	0
2-Chloroethanol (2CE)	0.46	0.53	1.28
1,2-dimethoxyethane (DME)	0.53	0.41	0
Toluene	0.54	0.11	0
Dichloromethane (DCM)	0.82	0.1	0.13
Acetone	0.71	0.43	0.08
Cyclohexanone (ChOH)	0.76	0.53	0
Ethyl acetate (EtAc)	0.55	0.45	0
Formamide (F)	0.97	0.48	0.71
Dimethylformamide (DMF)	0.88	0.69	0
Dimethylacetamide (DMAc)	0.88	0.76	0
1-Methyl-2-pyrrolidinone (NMP)	0.92	0.77	0
Acetonitrile (AcN)	0.75	0.4	0.19
Dimethylsulfoxide (DMSO)	1.00	0.76	0
Tetrahydrofuran (THF)	0.58	0.55	0
2-Pyrrolidone (2-Py)	0.85	0.77	0.36

Table S2. Values of Hammett sigma constants [3,4].

Substituent	σ
H	0.00
2-OH	-0.2
3-OH	0.12
4-OH	-0.37
2-O ⁻	-1.10
3-O ⁻	-0.47
4-O ⁻	-0.81
2-OMe	0.04
3-OMe	0.20
4-OMe	-0.27
2-Cl	0.79
3-Cl	0.37
4-Cl	0.40
2-I	0.31
3-I	0.35
4-I	0.18
2-NO ₂	0.95
3-NO ₂	0.71
4-NO ₂	0.78

2. Experimental

2.1. Materials

All commercially available chemicals were purchased from Sigma-Aldrich (St. Louis, MO, USA), and used without purification: isatin, aniline, 2-aminophenol, 3-aminophenol, 4-aminophenol, 2-methoxyaniline, 3-methoxyaniline, 4-methoxyaniline, 2-chloroaniline, 3-chloroaniline, 4-chloroaniline, 2-iodoaniline, 3-iodoaniline, 4-iodoaniline, 2-nitroaniline, 3-nitroaniline, 4-nitroaniline and glacial acetic acid. All used solvents were of spectroscopic quality (Sigma-Aldrich).

2.2. Synthesis and characterization of isatin derivatives

Isatin derivatives were synthesized according to the literature method [5] except compound 1,3-dihydro-3-(phenylimino)-2*H*-indol-2-one which synthesis was described in the previous study [6]. Isatin (5 mmol) was dissolved in methanol (40 mL), and

corresponding substituted anilines (5 mmol) and glacial acetic acid (10 mL) were added. Reaction mixture was refluxed at 70 °C for 6 h by using magnetic stirrer. Subsequently, the mixture was left overnight without stirring at room temperature. The obtained crystals were filtered off, dried and recrystallized from methanol or appropriate solvent mixture (Table S5). The average yield was about 60–79 %.

The most of synthesized compounds (**1-3**, **5-10**, **13**, **15** and **16**) are compared with those reported in earlier literature [5–11], and the other substances (**4**, **11**, **12** and **14**) are known compounds already published in literature [12,13] without NMR characterization, and therefore full data was given in Table S5.

Fourier-transform infrared (FTIR) spectra were recorded in transmission mode on BOMEM (Hartmann & Braun) instrument, MB series in the form of KBr pellets, and using ATR NICOLET iS10. FTIR spectra were recorded in the transmission mode between 400 and 4000 cm^{-1} with a resolution of 4 cm^{-1} . The purity of the obtained compounds was confirmed by elemental analysis. The FTIR characterization and elemental analysis are presented in Tables S3. and S4.

^1H and ^{13}C NMR characterizations were performed on a Varian Gemini 2000 (200/50 MHz) instrument at 25 °C. Chemical shifts (δ) were reported in part per million (ppm) relative to tetramethylsilane ($\delta_{\text{H}}=0$ ppm) in ^1H NMR, and to dimethyl sulfoxide ($\delta_{\text{C}}=39.5$ ppm) in ^{13}C NMR, using the residual solvent peak as a reference standard. 2D Nuclear Overhauser effect spectroscopy (NOESY), Heteronuclear Multiple Bond Correlation (HMBC) and Heteronuclear single quantum coherence spectroscopy (HSQC) spectra were recorded on a BrukerAvance 500 spectrometer (500/125 MHz) equipped with inverse detection triple resonance 5 mm probe (TXI). Standard pulse sequences were used for 2D spectra. The numeration of the atom of interest for characterization is given in Fig S1. UV data were obtained using Shimadzu 1700 UV-Vis spectrophotometer in appropriate solvent at $5 \times 10^{-5} \text{ mol dm}^{-3}$.

^1H and ^{13}C NMR spectra of studied compounds are given in Table S5, and general formula of studied isatin derivatives, with the labeling of atoms is given on Fig S1:

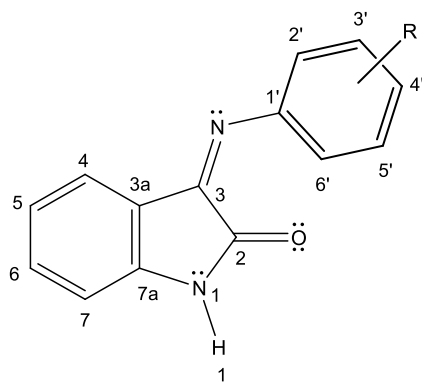


Figure S1. General formula of 1,3-dihydro-3-(substituted phenylimino)-2*H*-indol-2-ones with labeling of the atom.

Table S3. The list of synthesized isatin derivatives and results of elemental analysis.

Comp. No.	Compound	Substituent R	Elemental Analysis	
			Calculated	Found
1	1,3-dihydro-3-(phenylimino)-2 <i>H</i> -indol-2-one	H	%C, 75.66; %H, 4.54; %N, 12.60; %O, 7.20	%C, 75.61; %H, 4.57; %N, 12.61; %O, 7.21
2	1,3-dihydro-3-[(2-hydroxyphenyl)imino]-2 <i>H</i> -indol-2-one	2-OH	%C, 70.58; %H, 4.23; %N, 11.76; %O, 13.43	%C, 70.56; %H, 4.18; %N, 11.79; %O, 13.47
3	1,3-dihydro-3-[(3-hydroxyphenyl)imino]-2 <i>H</i> -indol-2-one	3-OH	%C, 70.58; %H, 4.23; %N, 11.76; %O, 13.43	%C, 70.59; %H, 4.19; %N, 11.78; %O, 13.44
4	1,3-dihydro-3-[(4-hydroxyphenyl)imino]-2 <i>H</i> -indol-2-one	4-OH	%C, 70.58; %H, 4.23; %N, 11.76; %O, 13.43	%C, 70.56; %H, 4.22; %N, 11.77; %O, 13.45
5	1,3-dihydro-3-[(2-methoxyphenyl)imino]-2 <i>H</i> -indol-2-one	2-OCH ₃	%C, 71.42; %H, 4.79; %N, 11.10; %O, 12.68	%C, 71.44; %H, 4.77; %N, 11.06; %O, 12.73
6	1,3-dihydro-3-[(3-methoxyphenyl)imino]-2 <i>H</i> -indol-2-one	3-OCH ₃	%C, 71.42; %H, 4.79; %N, 11.10; %O, 12.68	%C, 71.46; %H, 4.76; %N, 11.08; %O, 12.70
7	1,3-dihydro-3-[(4-methoxyphenyl)imino]-2 <i>H</i> -indol-2-one	4-OCH ₃	%C, 71.42; %H, 4.79; %N, 11.10; %O, 12.68	%C, 71.47; %H, 4.78; %N, 11.04; %O, 12.71
8	1,3-dihydro-3-[(2-chlorophenyl)imino]-2 <i>H</i> -indol-2-one	2-Cl	%C, 65.51; %H, 3.53; %Cl, 13.81; %N, 10.91; %O, 6.23	%C, 65.48; %H, 3.58; %Cl, 13.78; %N, 10.92; %O, 6.24
9	1,3-dihydro-3-[(3-chlorophenyl)imino]-2 <i>H</i> -indol-2-one	3-Cl	%C, 65.51; %H, 3.53; %Cl, 13.81; %N, 10.91; %O, 6.23	%C, 65.45; %H, 3.59; %Cl, 13.78; %N, 10.88; %O, 6.30
10	1,3-dihydro-3-[(4-chlorophenyl)imino]-2 <i>H</i> -indol-2-one	4-Cl	%C, 65.51; %H, 3.53; %Cl, 13.81; %N, 10.91; %O, 6.23	%C, 65.47; %H, 3.57; %Cl, 13.79; %N, 10.93; %O, 6.24
11	1,3-dihydro-3-[(2-iodophenyl)imino]-2 <i>H</i> -indol-2-one	2-I	%C, 48.30; %H, 2.61; %I, 36.45; %N, 8.05; %O, 4.60	%C, 48.26; %H, 2.64; %I, 36.40; %N, 8.07; %O, 4.63
12	1,3-dihydro-3-[(3-iodophenyl)imino]-2 <i>H</i> -indol-2-one	3-I	%C, 48.30; %H, 2.61; %I, 36.45; %N, 8.05; %O, 4.60	%C, 48.34; %H, 2.62; %I, 36.39; %N, 8.03; %O, 4.62
13	1,3-dihydro-3-[(4-iodophenyl)imino]-2 <i>H</i> -indol-2-one	4-I	%C, 48.30; %H, 2.61; %I, 36.45; %N, 8.05; %O, 4.60	%C, 48.28; %H, 2.63; %I, 36.42; %N, 8.03; %O, 4.64
14	1,3-dihydro-3-[(2-nitrophenyl)imino]-2 <i>H</i> -indol-2-one	2-NO ₂	%C, 62.92; %H, 3.39; %N, 15.72; %O, 17.96	%C, 62.86; %H, 3.42; %N, 15.75; %O, 17.97
15	1,3-dihydro-3-[(3-nitrophenyl)imino]-2 <i>H</i> -indol-2-one	3-NO ₂	%C, 62.92; %H, 3.39; %N, 15.72; %O, 17.96	%C, 62.94; %H, 3.40; %N, 15.74; %O, 17.92
16	1,3-dihydro-3-[(4-nitrophenyl)imino]-2 <i>H</i> -indol-2-one	4-NO ₂	%C, 62.92; %H, 3.39; %N, 15.72; %O, 17.96	%C, 62.93; %H, 3.39; %N, 15.72; %O, 17.96

Table S4. FTIR Characterization of investigated isatin derivatives.

R	IR (KBr) ν_{\max} (cm⁻¹)
H	3194.86 (N-H amide group stretching), 1713.57 (C=O amide stretching), 1613.91 (C=N imino stretching).
2-OH	3124.42 (N-H amide group stretching), 1716.82 (C=O amide stretching), 1613.54 (C=N imino stretching), 1342.60 (hydroxyl C-O stretching).
3-OH	3128.74 (N-H amide group stretching), 1722.99 (C=O amide stretching), 1614.77 (C=N imino stretching), 1341.56 (hydroxyl C-O stretching).
4-OH	3194.86 (N-H amide group stretching), 1725.83 (C=O amide stretching), 1610.31 (C=N imino stretching), 1332.82 (hydroxyl C-O stretching).
2-OMe	3461.30 (N-H amide group stretching), 1745.31 (C=O amide stretching), 1605.52 (C=N imino stretching), 1193.36 (methoxy C-O stretching).
3-OMe	3436.62 (N-H amide group stretching), 1735.83 (C=O amide stretching), 1602.19 (C=N imino stretching), 1183.44 (methoxy C-O stretching).
4-OMe	3462.29 (N-H amide group stretching), 1745.33 (C=O amide stretching), 1604.03 (C=N imino stretching), 1193.69 (methoxy C-O stretching).
2-Cl	3189.86 (N-H amide group stretching), 1724.17 (C=O amide stretching), 1613.47 (C=N imino stretching), 660.23 (C-Cl stretching).
3-Cl	3189.99 (N-H amide group stretching), 1724.11 (C=O amide stretching), 1613.63 (C=N imino stretching), 660.01 (C-Cl stretching).
4-Cl	3189.99 (N-H amide group stretching), 1724.39 (C=O amide stretching), 1613.14 (C=N imino stretching), 660.09 (C-Cl stretching).
2-I	3190.00 (N-H amide group stretching), 1727.09 (C=O amide stretching), 1613.33 (C=N imino stretching), 661.26 (C-I stretching).
3-I	3189.30 (N-H amide group stretching), 1724.02 (C=O amide stretching), 1613.35 (C=N imino stretching), 660.49 (C-I stretching).

4-I	3161.24 (N-H amide group stretching), 1722.15 (C=O amide stretching), 1604.59 (C=N imino stretching), 652.49 (C-I stretching).
2-NO₂	3189.73 (N-H amide group stretching), 1746.57 (C=O amide stretching), 1613.17 (C=N imino stretching), 1330.96 (nitro C-NO ₂ stretching).
3-NO₂	3178.65 (N-H amide group stretching), 1746.69 (C=O amide stretching), 1608.75 (C=N imino stretching), 1336.95 (nitro C-NO ₂ stretching).
4-NO₂	3192.21 (N-H amide group stretching), 1745.24 (C=O amide stretching), 1614.67 (C=N imino stretching), 1330.74 (nitro C-NO ₂ stretching).

Table S5. Yield, melting point, ^1H and ^{13}C NMR data of synthesized compounds.

No	Yield; m.p. solvent mixture used for recrystallization	Ratio <i>E:Z</i> isomers	^1H NMR (500 MHz, DMSO- d_6)(ppm)	^{13}C NMR (125 MHz, DMSO- d_6)(ppm)
4	72 %; 182-184 °C (methanol)	7.5:2.5	Isomer E 6.70 (d, 1H, 4), 6.75 (dd, 2H, 2',6'), 6.80-6.94 (m, 3H, 5,6,7), 7.33 (td, 2H, 3', 5'), 9.57 (s, 1H, 4'-OH), 10.92 (s, 1H, N1-H); Isomer Z 6.77 (td, 1 H, $J = 8.2, 1.0$), 7.01-7.09 (m, 3 H, H-5, H-2', H-5'), 7.35-7.45 (m, $J = 7.8, 1.2$ Hz, 2 H, H-3', H-5'), 7.53 (td, $J = 7.7$ Hz, 1 H, H-6), 7.61-7.66 (m, H-4), 10.81 (s, 1 H, N1-H).	Isomer E 111.65 (C-7), 116.12 (C-3a), 120.09 (C-2', C-6'), 122.33 (C-5), 125.09 (C-4), 134.28 (C-6), 139.64 (C-3', C-5'), 144.92 (C-7a), 146.52 (C-1'), 155.73 (C-3), 156.64 (C-4'), 164.06 (C-2); Isomer Z 115.00 (C-7), 116.20 (C-3a), 121.921 (C-2', C-6'), 124.12 (C-5), 125.14 (C-4), 141.85 (C-6), 142.64 (C-3', C-5'), 143.92 (C-7a), 144.93 (C-1'), 154.29 (C-3), 155.21 (C-4'), 159.09 (C-2).
5	69 %; 190-191 °C (DMSO/methanol)	7.5:2.5	Isomer E 3.69 (s, 3H, OCH ₃), 6.43 (d, H-4), 6.74 (m, H-5, H-7; 2H), 6.92 (d, $J = 8.8$ Hz, 1 H, H-2'), 7.01 (dd, 1 H, H-3'), 7.34 (t, 1 H, H-6), 10.98 (br s, 1 H, N1-H); Isomer Z 3.77 (s, 3H, OCH ₃), 6.87 (d, 2 H, H-4, H-3'), 7.08 (d, 1 H, H-5), 7.14 (d, 1 H, H-2'), 7.47 (dd, 1 H, H-6), 7.59 (m, 1 H, H-7), 10.81 (br s, 1 H, N1-H);	Isomer E 55.59 (OCH ₃), 111.74 (C-7), 115.58 (C-3'), 117.71 (C-3a), 118.72 (C-2'), 121.15 (C-5), 125.0 (C-4), 134.77 (C-6), 147.85 (C-7a), 151.00 (C-1'), 155.87 (C-3), 159.69 (C-4'), 163.83 (C-2); Isomer Z 55.73 (OCH ₃), 111.10 (C-7), 112.51 (C-3'), 116.61 (C-3a), 122.28 (C-5), 122.66 (C-4), 123.09 (C-2'), 134.55 (C-6), 146.44 (C-7a), 148.39 (C-1'), 154.35 (C-3), 159.12 (C-4'), 159.69 (C-2).
7	61 %; 238-240 °C (DMSO/methanol)	8:2	Isomer E 3.79 (s, 3H, OCH ₃), 6.64 (dd, $J = 7.8, 0.6$ Hz, 1 H, H-4), 6.75 (td, $J = 7.7, 1.1$ Hz, 1 H, H-5), 6.88 (dm, $J = 7.2$ Hz, 1 H, H-7), 6.97 (d, $J = 8.8$ Hz, 2 H, H-2', H-6'), 7.03 (d, $J = 8.8$ Hz, 2 H, H-3', H-5'), 7.33 (td, $J = 7.8, 1.2$ Hz, 1 H, H-6), 10.91 (br s, 1 H, N1-H); Isomer Z 3.77 (s, 3H, OCH ₃), 6.83 (d, $J = 8$ Hz, 1 H, H-4), 6.89 (masked d, 1 H, H-3', H-5'), 7.03 (masked t, 1 H, H-5), 7.17 (d, $J = 8.8$ Hz, 2 H, H-2', H-6'), 7.40 (td, $J = 7.6, 1.2$ Hz, 1 H, H-6), 7.55 (dd, $J = 7.6, 0.4$ Hz, 1 H, H-7), 10.91 (br s, 1 H, N1-H).	Isomer E 55.5 (OCH ₃), 111.6 (C-7), 114.9 (C-3'), 116.0 (C-3a), 119.6 (C-2'), 121.9 (C-5), 125.1 (C-4), 134.4 (C-6), 143.3 (C-1'), 147.0 (C-7a), 154.7 (C-3), 157.3 (C-4'), 163.8 (C-2); Isomer Z 55.5 (OCH ₃), 110.7 (C-7), 113.6 (C-3'), 114.9 (C-3a), 122.3 (C-5), 122.5 (C-4), 122.9 (C-2'), 133.7 (C-6), 141.2 (C-1'), 145.2 (C-7a), 151.8 (C-3), 157.7 (C-4'), 158.9 (C-2).
10	72 %; 216-218 °C (methanol)	7.5:2.5	Isomer E 6.43 (dd, $J = 7.7, 0.6$ Hz, 1 H, H-4), 6.77 (td, $J = 7.7, 0.9$ Hz, 1 H, H-5), 6.90 (d, $J = 7.8$ Hz, 1 H, H-7), 7.00-7.05 (m, 2 H, H-2', H-6'), 7.34 (m, 1 H, H-6), 7.51 (m, 2 H, H-3', H-5'), 10.99 (s, 1 H, N1-H); Isomer Z 6.87 (d, $J = 7.8$ Hz, 1 H, H-4), 7.01-7.05 (m, 2 H, H-2', H-5') 7.07 (dd, $J = 7.6, 0.8$ Hz, 1 H, H-5), 7.34 (m, 1 H, H-3'), 7.37 (d, $J = 1.2$ Hz, 1 H, H-5'), 7.45 (td, $J = 7.7, 1.3$ Hz, 1 H, H-6), 7.58 (dd, $J = 7.5,$	Isomer E 111.67 (C-4'), 119.37 (C-7), 120.96 (C-3a), 121.94 (C-2'), 122.99 (C-5), 125.47 (C-4), 134.75 (C-6), 138.43 (C-3'), 147.14 (C-7a), 149.23 (C-1'), 155.40 (C-3), 163.39 (C-2); Isomer Z 110.89 (C-4'), 115.63 (C-7), 119.45 (C-3a), 121.24 (C-2'), 122.43 (C-5), 124.73 (C-4), 134.50 (C-6), 137.46 (C-3'), 145.88 (C-7a), 147.95 (C-1'), 153.67 (C-3), 158.56 (C-2).

11	77 %; 172-174 °C (DMF/methanol)	8:2	0.6 Hz H-4), 10.88 (s, 1 H, N1-H). Isomer E 6.19 (d, 1H, 4), 6.70 (t, 1H, 5), 6.86-7.08 (m, 3H, 6,5',7), 7.43 (dd, 2H, 4',6'), 7.96 (d, 1H, 3'), 11.05 (s, 1H, N1-H); Isomer Z 6.90 – 7.15 (d, 2 H, H-4, H-3'), 7.08 (d, 1 H, H-5), 7.13 (d, 1 H, H-2'), 7.42 (dd, 1 H, H-6), 7.54 (m, 1 H, H-7), 10.94 (br s, 1 H, N1-H).	Isomer E 86.35 (C-2'), 111.76 (C-7), 116.14 (C-3a), 118.75 (C-6'), 122.78 (C-5'), 123.28 (C-5), 125.84 (C-4), 129.11 (C-4'), 135.53 (C-6), 138.69 (C-3'), 147.32 (C-7a), 152.48 (C-1'), 156.72 (C-3), 164.17 (C-2); Isomer Z 86.35 (C-2'), 112.06 (C-7), 116.12 (C-3a), 118.73 (C-6'), 121.99 (C-5'), 123.22 (C-5), 125.77 (C-4), 129.03 (C-4'), 135.41 (C-6), 138.43 (C-3'), 147.12 (C-7a), 151.66 (C-1'), 154.57 (C-3), 158.70 (C-2).
12	70 %; 247.9 °C (DMF/methanol)	7:2	Isomer E 6.35(d, 1H, 4), 6.77 (t, 1H, 5), 6.89 (d, 1H, 7), 6.92-7.03 (m, 2H, 6, 4'), 7.26 (t, 1H, 5'), 7.38-7.61 (dd, 2H, 2',6'), 10.98 (s, 1H, N1-H); Isomer Z 6.95 – 7.16 (d, 2 H, H-4, H-3'), 7.06 (d, 1 H, H-5), 7.12 (d, 1 H, H-2'), 7.45 (dd, 1 H, H-6), 7.56 (m, 1 H, H-7), 10.86 (br s, 1 H, N1-H).	Isomer E 94.47 (C-3'), 111.98 (C-7), 117.21 (C-3a), 118.74 (C-6'), 122.18 (C-5'), 123.35 (C-5), 125.74 (C-4), 130.71 (C-4'), 134.89 (C-6), 135.09 (C-3'), 147.47 (C-7a), 152.21 (C-1'), 155.82 (C-3), 163.64 (C-2); Isomer Z 90.01 (C-3'), 111.0 (C-7), 121.2 (C-3a), 121.5 (C-2'), 122.8 (C-5), 122.9 (C-4), 135.1 (C-6), 137.1 (C-4'), 145.9 (C-7a), 151.04 (C-1'), 153.97 (C-3), 158.7 (C-2).
13	61 %; 269.3 °C (DMF/methanol)	7.5:2.5	Isomer E 6.44 (d, $J = 7.6$ Hz, 1 H, H-4), 6.74 (td, $J = 7.7, 0.6$, 1 H, H-5), 6.83 (d, $J = 8.8$ Hz, 2 H, H-3', H-5'), 6.88 (d, $J = 8$ Hz, 1 H, H-7), 7.35 (td, $J = 7.6, 1.2$ Hz, 2 H, H-2', H-6'), 7.79 (d, $J = 8.4$ Hz, 2 H, H-3), 10.97 (s, 1 H, N1-H); Isomer Z 6.80-6.87 (m, 3 H, H-7 and H-2'), 7.05 (t, $J = 7.2$ Hz, 1 H, H-5), 7.45 (td, $J = 7.8, 1.2$ Hz, 1 H, H-5), 7.45 (td, $J = 7.8, 1.2$ Hz, 1 H, H-6), 7.57 (d, $J = 7.2$ Hz, 1 H, H-4), 7.62 (d, $J = 8.8$ Hz, 2 H, H-3'), 10.87 (s, 1 H, N1-H).	Isomer E 88.4 (C-4'), 111.8 (C-7), 115.8 (C-3a), 120.1 (C-2'), 122.0 (C-5), 125.6 (C-4), 134.9 (C-6), 138.4 (C-3'), 147.3 (C-7a), 150.2 (C-1'), 155.3 (C-3), 163.5 (C-2); Isomer Z 88.9 (C-4'), 111.0 (C-7), 121.4 (C-3a), 121.6 (C-2'), 122.5 (C-5), 123.1 (C-4), 134.6 (C-6), 137.2 (C-3'), 146.0 (C-7a), 149.1 (C-1'), 153.5 (C-3), 158.7 (C-2).
14	65 %; 195-197 °C (DMF/methanol)	1:0	Isomer E 6.60 (ddd, 1H, 4), 6.90 (t, 1H, 5), 7.00 (dd, 1H, 6), 7.10 (t, 1H, 5'), 7.38 – 7.55 (m, 3H, 7,4',6'), 7.60 (d, 1H, 4'), 7.95 (dd, 1H, 3'), 11.03 (s, 1H, N1-H).	Isomer E 112.45 (C-7), 115.72 (C-3a), 118.08 (C-6'), 119.43 (C-5'), 123.02 (C-5), 124.95 (C-4), 125.63 (C-4'), 130.53 (C-6), 135.90 (C-3'), 145.98 (C-7a), 145.85 (C-1'), 150.43 (C-3), 159.04 (C-2), 184.86 (C-2').
16	60 %; 238-240 °C (DMF/methanol)	1:0	E isomer: 6.62 (d, 1H, 4), 6.90 (dd, 2H, 2',6'), 6.95-7.08 (m, 2H, 5,6), 7.56 (dd, 1 H, 7), 7.90 (ddd, 2H, 3', 5'), 11.04 (s, 1H, N1-H).	E isomer: 112.43 (C-7), 112.61 (C-3a), 118.07 (C-2', C-6'), 123.00 (C-5), 124.94 (C-4), 126.66 (C-6), 135.87 (C-3', C-5'), 138.62 (C-7a), 150.97 (C-1'), 155.96 (C-3), 159.63 (C-2), 184.67 (C-4').

Table S6. ^1H and ^{13}C NMR data of appropriate carbon used in LFER correlation and ratio of *E/Z* isomer.

Substituent/ form	N-H	C2=O	C3=N3	C1'	Reference	Ratio of isomer
H / E	10.76	163.50	156.65	151.67	-	<i>E/Z</i> = 8:2
H / Z	10.64	158.97	155.10	148.96	-	
2-OH / E	10.94	163.95	155.80	146.62	-	<i>E/Z</i> = 8:2
2-OH / Z	10.80	159.64	150.90	145.62		
3-OH / E	10.10	164.0	155.0	139.0	[8]	<i>E</i>
4-OH / E	10.92	164.06	155.73	146.52	-	<i>E/Z</i> = 7.5:2.5
4-OH / Z	10.81	159.09	154.29	144.93		
2-OMe / E	10.98	163.83	155.87	151.0	-	<i>E/Z</i> = 7.5:2.5
2-OMe / Z	10.81	159.69	154.35	148.39		
3-OMe / E	10.97	164.0	155.0	147.0	[8]	<i>E</i>
4-OMe / E	10.91	163.8	154.7	143.3	[9]	<i>E/Z</i> = 8:2
4-OMe / Z	10.91	158.9	151.8	141.2	[9]	
2-Cl / E	11.04	163.42	156.63	150.95	-	<i>E/Z</i> = 8:2
2-Cl / Z	10.92	158.52	155.16	147.59	-	
3-Cl / E	11.04	163.57	155.94	150.97	-	<i>E/Z</i> = 8:2
3-Cl / Z	10.91	159.63	154.10	147.45	-	
4-Cl / E	11.00	163.39	155.40	149.23	-	<i>E/Z</i> = 7.5:2.5
4-Cl / Z	10.88	158.56	153.67	147.95		
2-I / E	11.05	164.17	156.72	152.48	-	<i>E/Z</i> = 8:2
2-I / Z	10.94	158.70	154.57	151.66		
3-I / E	10.98	163.64	155.82	152.21	-	<i>E/Z</i> = 7:2
3-I / Z	10.86	158.81	153.97	151.04		
4-I / E	10.97	163.5	155.3	150.2	[9]	<i>E/Z</i> = 7.5:2.5
4-I / Z	10.87	158.7	153.5	149.1	[9]	
2-NO₂ / E	11.03	159.04	150.43	145.85	-	<i>E</i>
3-NO₂ / E	10.99	163.79	155.48	147.33	-	<i>E/Z</i> = 7:2
3-NO₂ / Z	10.88	158.79	153.33	145.99		
4-NO₂ / E	11.04	159.63	155.96	150.97	-	<i>E</i>

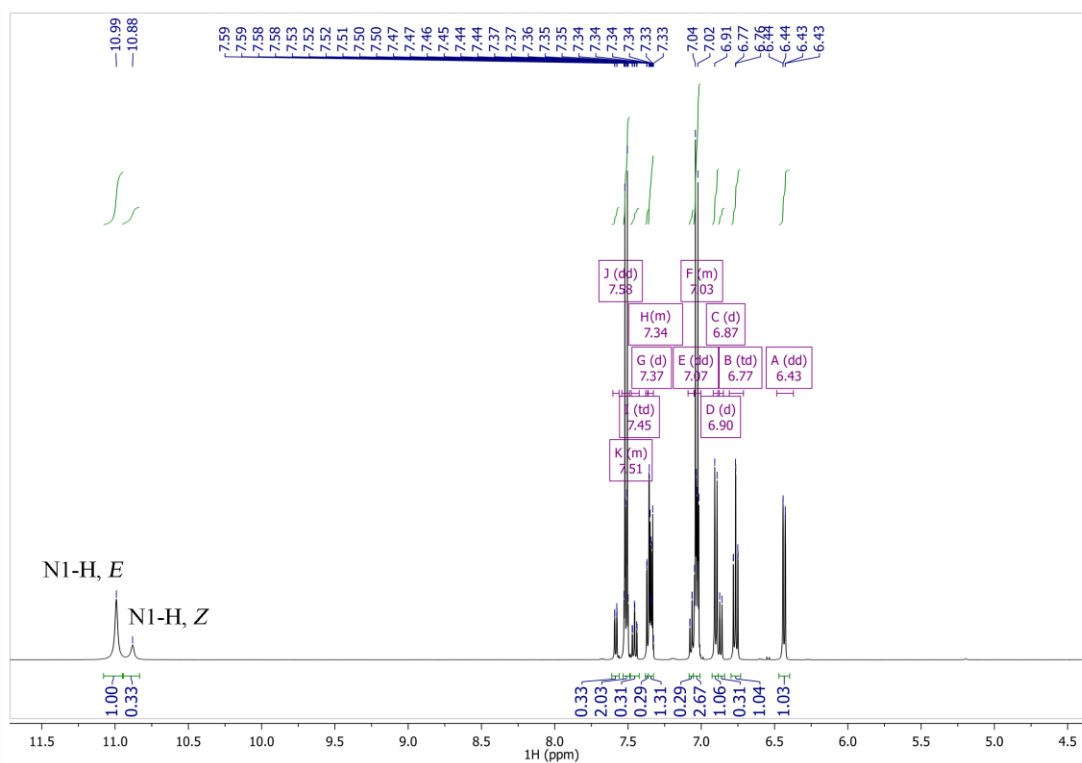


Figure S2. ^1H NMR spectrum of compound **10** in $\text{DMSO-}d_6$.

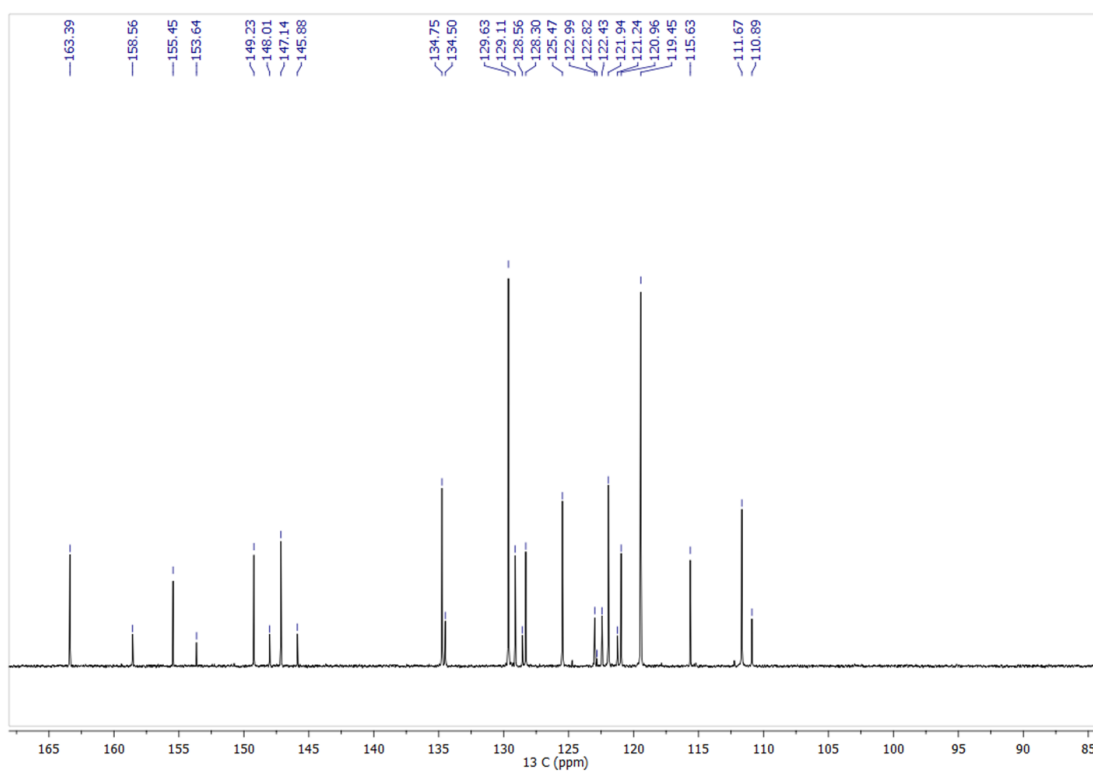


Figure S3. ^{13}C NMR spectrum of compound **10** in $\text{DMSO-}d_6$.

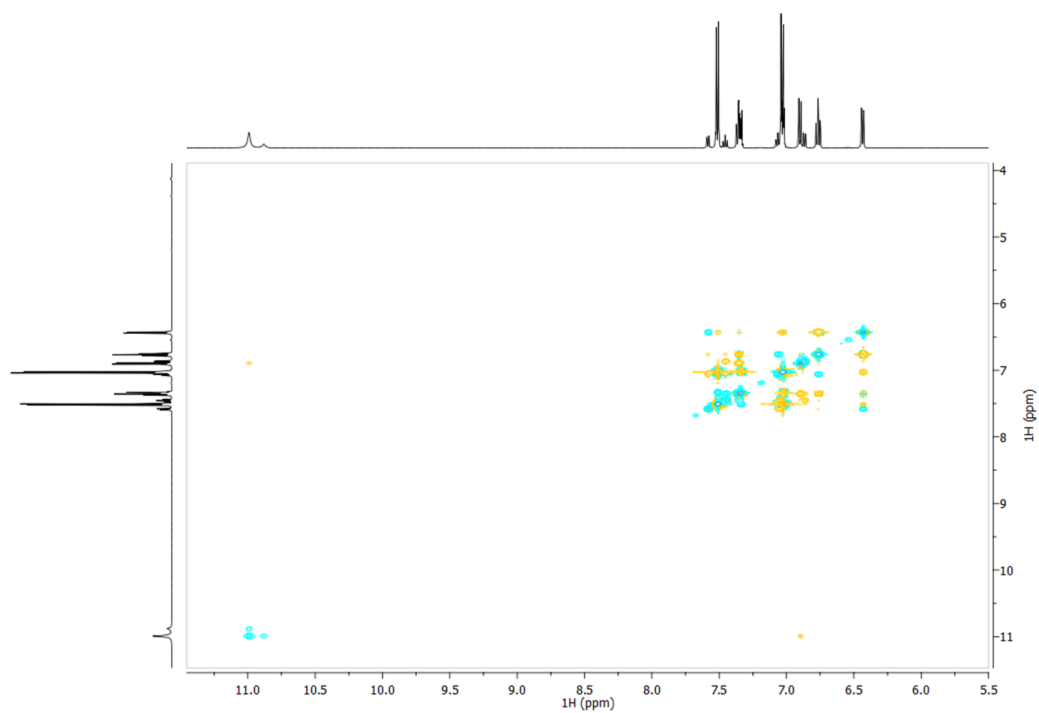


Figure S4. COSY spectrum of compound **10** in DMSO- d_6 .

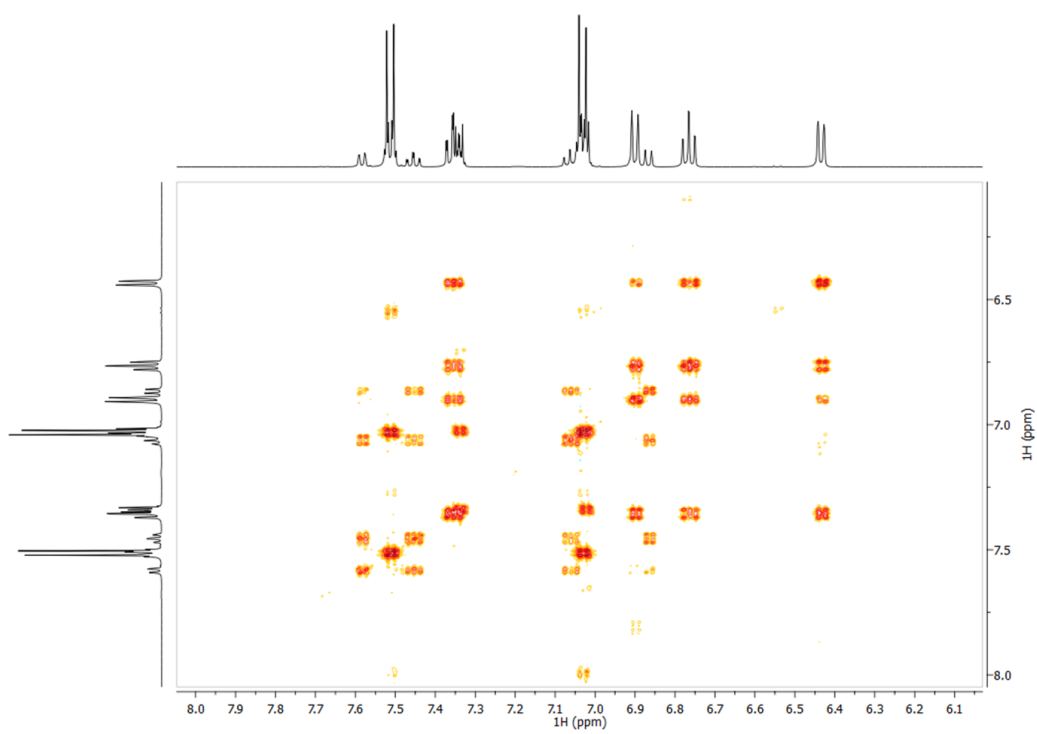


Figure S5. NOESY spectrum of compound **10** in DMSO- d_6 .

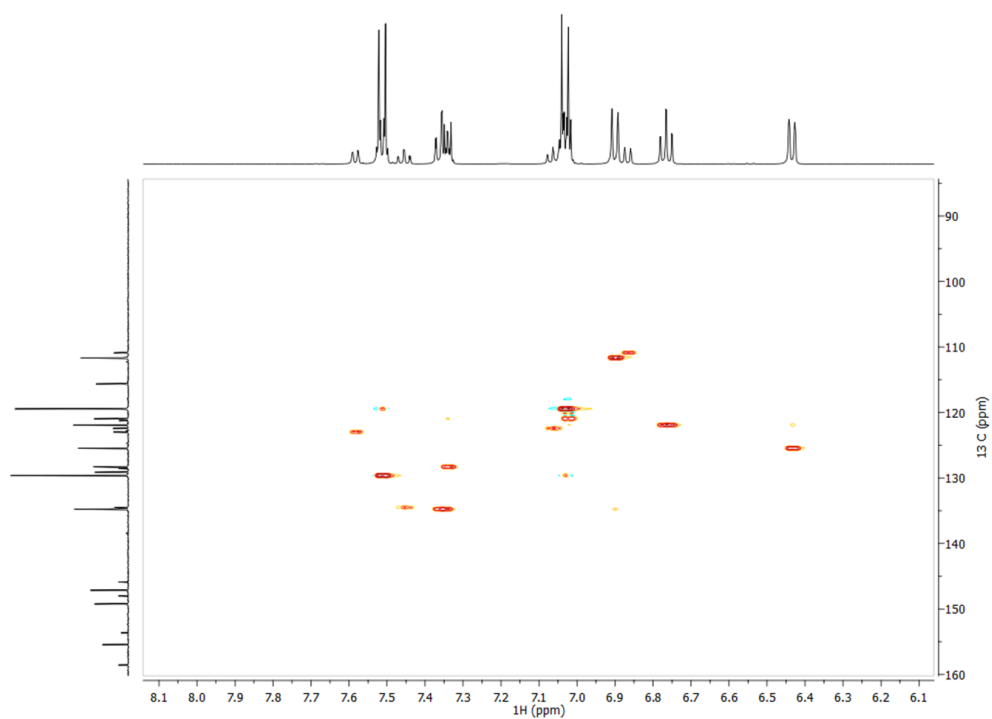


Figure S6. ^1H - ^{13}C HSQC spectrum of compound **10** in $\text{DMSO-}d_6$.

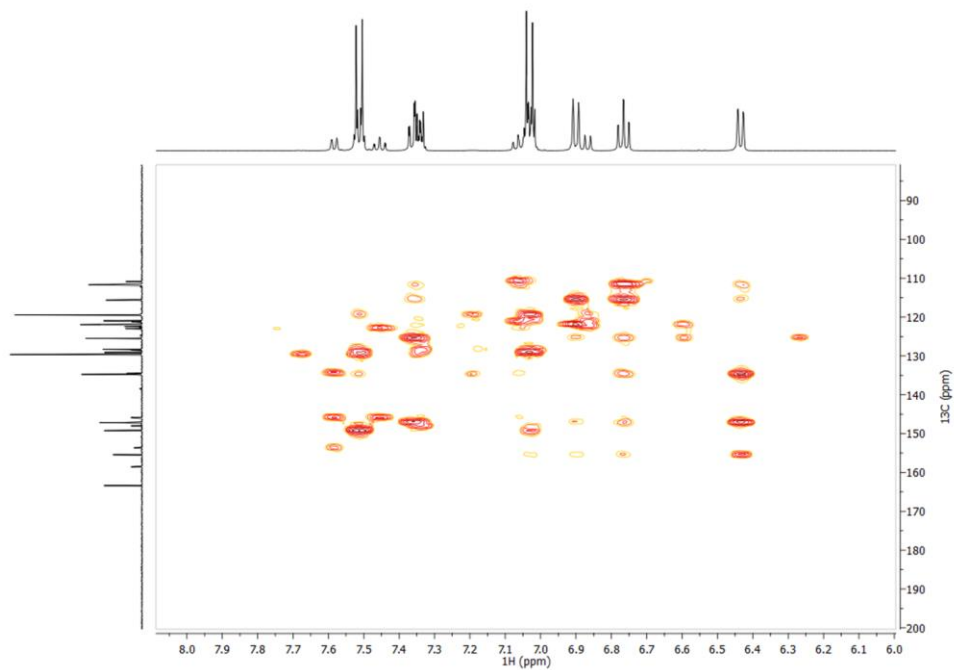


Figure S7. ^1H - ^{13}C HMBC spectrum of compound **10** in $\text{DMSO-}d_6$.

3. Results and discussion

3.2. Determination of acidity constants

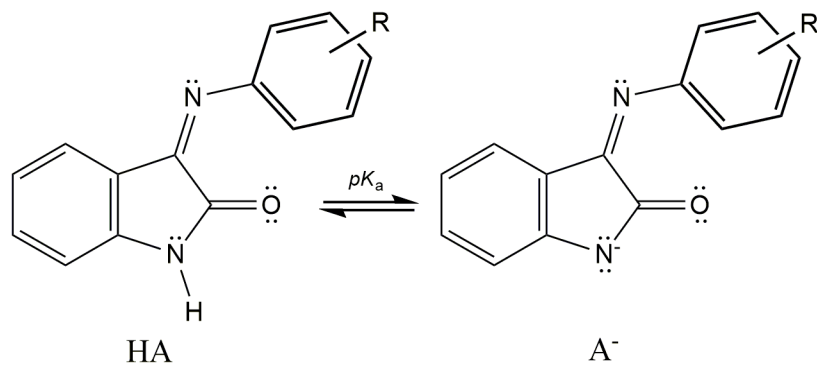


Figure S8. Protolytic equilibria of isatin derivatives in aqueous media.

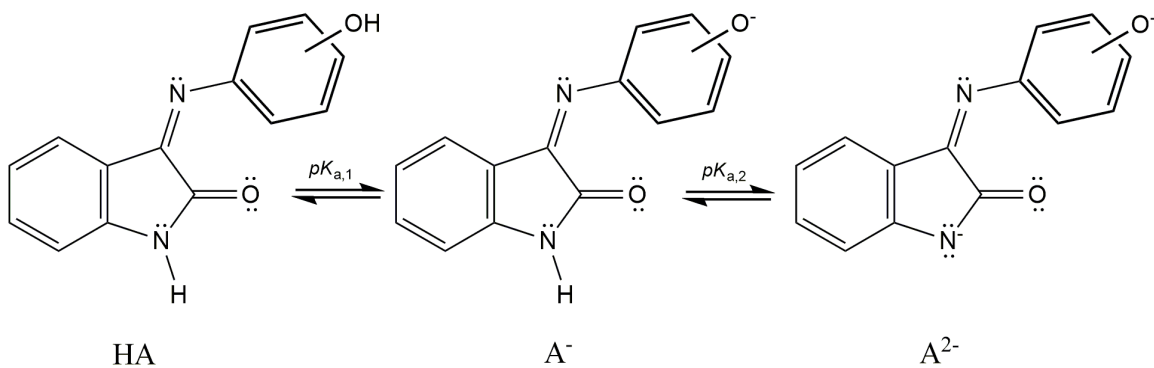


Figure S9. Protolytic equilibria of hydroxy substituted isatin derivatives in aqueous media (comps. 2–4).

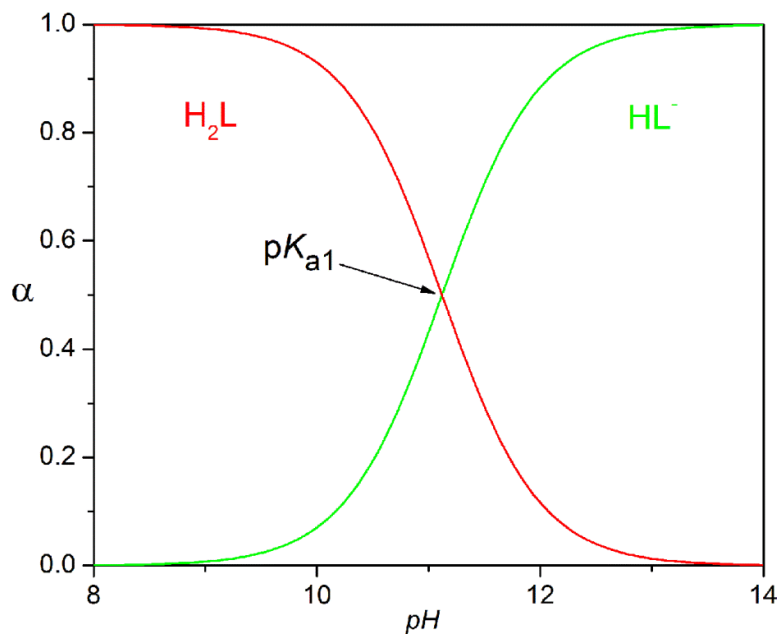


Figure S10. Isatin derivatives distribution diagram for non-hydroxy substituted compounds, example given for compound **16**. Species notation as in Fig S8.

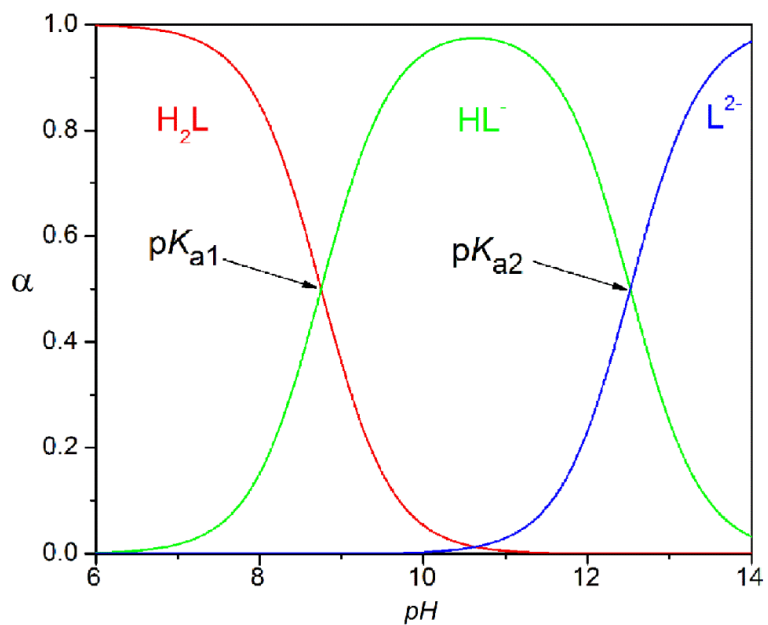


Figure S11. Isatin derivatives distribution diagram for hydroxi substituted compounds, example given for compound **2**. Species notation as in Fig S9.

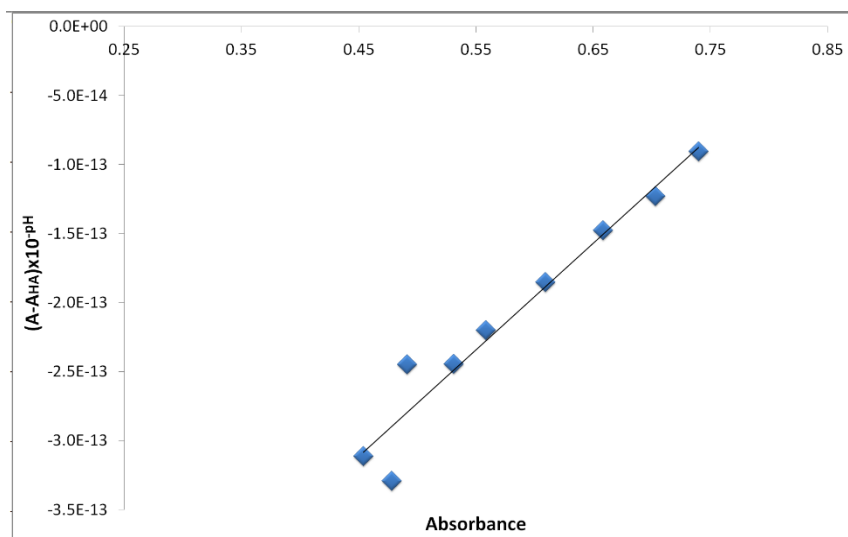


Figure S12. Determination of K_a for compound **16** at 380 nm according to Eq. 4a; slope = 7.72×10^{-13} , intercept = -6.594×10^{-13} , $r = 0.972$.

3.3. Solvent effects on the UV spectra

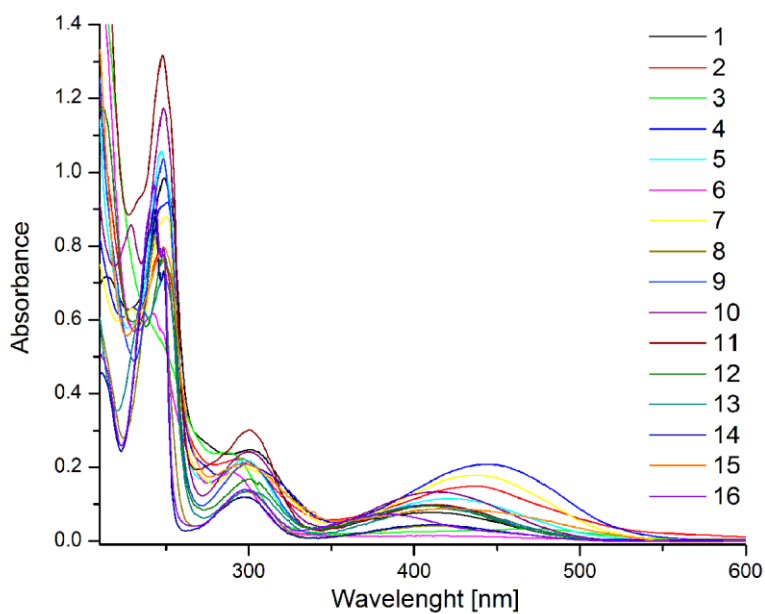


Figure S13. Absorption spectra of compounds **1 - 16** in ethanol.

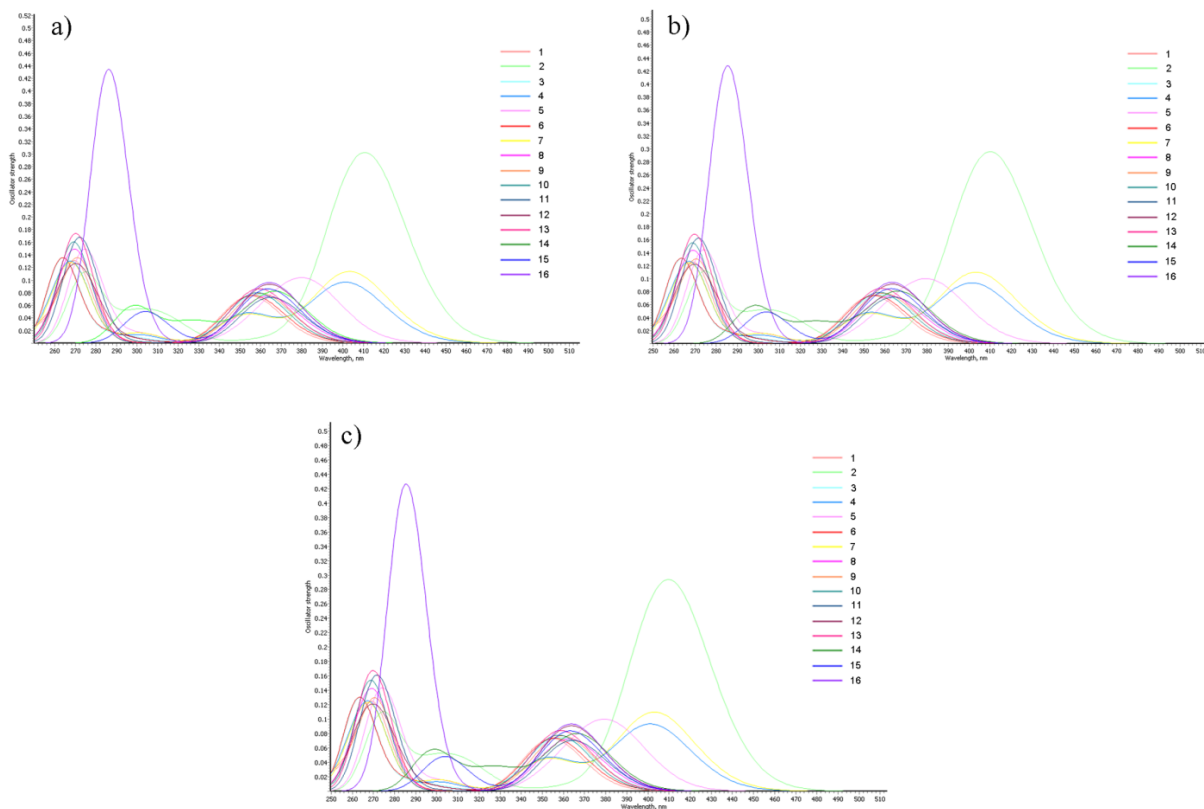


Figure S14. TD-DFT calculated UV-Vis spectra of *E* isomers form in a) DMSO, b) EtOH, c) AcN.

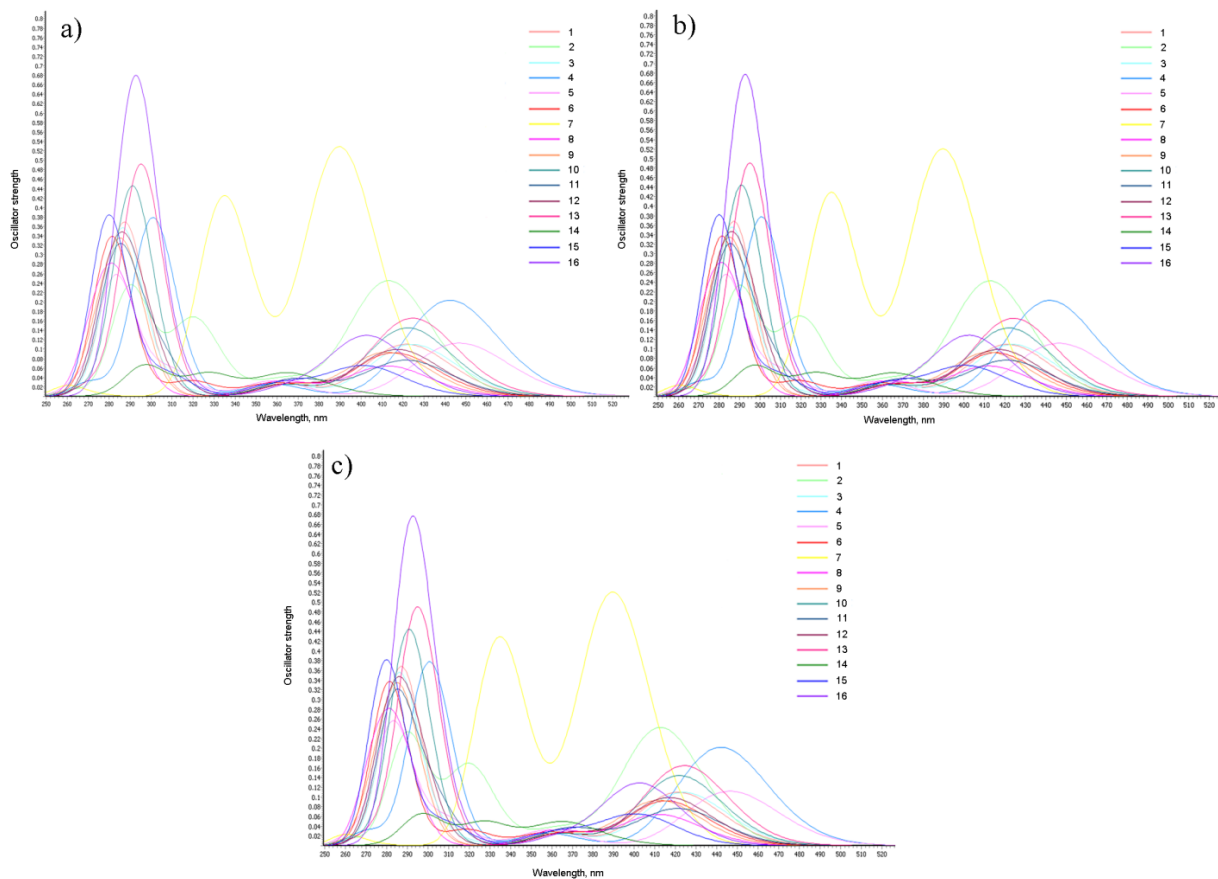


Figure S15. TD-DFT calculated UV-Vis spectra of Z isomers form in a) DMSO, b) EtOH, c) AcN.

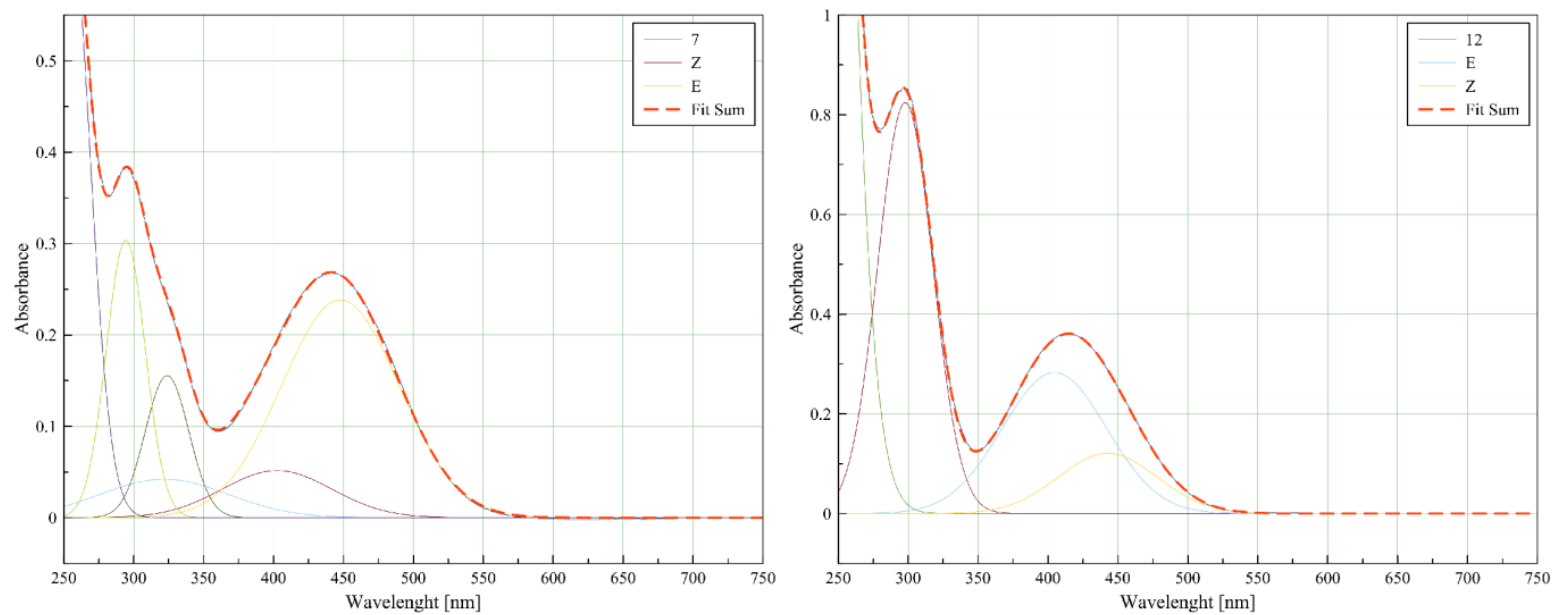


Figure S16. Deconvolution of overlapped bands of compounds **7** and **12** in DMSO.

Table S7. Absorption frequencies of isatin compounds in selected solvents for Z isomer.

Solvent/ Comp.	$\nu_{\max} \times 10^{-3} \text{ (cm}^{-1}\text{)}$															
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
MeOH	23.87	23.53	21.45	21.68	22.66	22.74	26.41	23.45	23.36	23.16	22.33	23.14	22.11	26.17	23.03	22.39
EtOH	23.27	22.14	20.85	21.52	22.15	23.65	25.04	22.93	22.71	22.78	23.31	23.19	22.87	24.97	22.66	21.85
2-PrOH	23.05	21.96	21.39	21.51	22.44	21.58	25.65	22.52	22.97	22.42	22.99	22.95	22.77	25.02	22.71	21.77
2-BuOH	20.70	22.33	21.25	21.35	22.38	24.42	24.81	22.33	21.72	21.35	20.96	22.09	21.58	24.74	22.84	21.64
ChOH	22.27	22.36	20.52	21.72	22.85	21.24	25.06	21.83	22.12	22.21	20.86	22.74	21.91	25.03	23.23	21.55
BzOH	22.91	22.23	20.78	21.58	21.65	22.81	25.07	21.72	22.71	22.39	21.35	22.61	21.65	25.05	22.92	22.41
2ME	/	22.96	/	21.87	21.64	/	24.62	22.23	23.17	22.81	22.73	23.32	21.78	25.23	22.87	22.61
2CE	23.08	20.47	19.68	19.13	21.41	23.65	22.61	21.34	22.81	22.24	22.06	21.92	22.07	27.07	22.33	21.79
DME	22.09	23.35	20.79	21.37	22.38	23.07	25.29	21.43	22.99	21.61	22.91	22.36	21.07	25.66	21.69	23.20
Toluene	22.49	20.93	19.58	19.77	21.03	23.30	23.49	22.27	21.88	21.28	20.8	21.12	21.06	25.09	22.38	21.46
DCM	23.24	22.57	/	21.78	22.31	23.92	24.52	22.66	22.52	22.94	22.53	22.51	22.51	24.87	/	21.88
Acetone	22.26	23.28	21.36	21.77	22.29	21.87	24.62	21.61	22.06	21.71	21.49	21.71	20.98	25.46	22.34	22.48
ChO	21.69	23.16	21.34	21.72	21.49	22.51	24.61	21.79	22.54	22.48	21.03	21.33	22.02	26.56	21.84	22.79
EtAc	21.78	22.41	20.79	21.50	21.77	21.32	25.30	22.01	22.54	21.15	23.16	21.21	21.11	26.30	/	23.98
F	23.18	23.16	20.59	21.30	22.37	22.65	25.63	22.79	22.88	22.7	22.92	23.05	23.02	24.48	22.76	21.66
DMF	23.07	23.03	19.99	21.22	22.26	22.07	24.59	21.21	21.79	21.69	22.42	21.57	22.26	24.41	22.15	21.96
DMAc	22.16	23.35	20.57	21.33	20.26	21.15	24.77	20.99	22.84	21.93	22.19	21.54	22.14	24.62	22.38	21.96
NMP	22.24	23.21	20.28	20.60	22.03	23.03	25.34	21.12	22.65	22.03	21.98	22.09	22.26	24.09	21.99	21.82
AcN	23.68	23.51	22.08	21.73	22.28	22.81	25.26	22.60	23.61	22.71	22.91	22.99	22.86	25.28	22.70	22.72
DMSO	23.22	23.09	20.99	21.34	22.21	24.12	24.84	22.78	22.51	22.12	22.21	22.59	22.16	24.46	22.00	24.36
THF	21.78	22.75	21.07	21.30	21.56	20.80	24.38	22.33	21.91	21.44	21.74	21.45	22.83	25.93	21.60	23.27
2-Py	22.74	22.89	20.14	21.11	22.67	23.39	24.32	21.14	22.38	22.47	20.98	22.86	22.23	24.13	22.02	21.80

3.4. LSER analysis of UV data

Table S8. Results of the correlation analysis the for *Z* isomers according to Kamlet–Taft equation.

Comp.	$\nu_0 \times 10^{-3}$ (cm^{-1})	$s \times 10^{-3}$ (cm^{-1})	$b \times 10^{-3}$ (cm^{-1})	$a \times 10^{-3}$ (cm^{-1})	R^a	Sd^b	F^c	P_π^d	P_β	P_α	Solvent excluded from correlation
1	22.06 ±0.31	0.25 ±0.38	-0.38 ±0.39	1.67 ±0.20	0.943	0.247	26.93	10.87	16.52	72.61	2ME, 2-BuOH, AcN, DMSO, DMF, 2-CE, DCM, ChO
2	23.00 ±0.35	-0.20 ±0.41	0.63 ±0.28	-1.81 ±0.21	0.943	0.267	34.59	7.58	23.86	68.56	MeOH, Toluene, F, EtAc, AcN
3	21.45 ±0.25	-3.94 ±0.43	3.24 ±0.34	-1.29 ±0.18	0.966	0.182	36.87	46.52	38.25	15.23	2ME, DCM, AcN, MeOH, Acetone, BzOH, F, ChO, ChO, DMSO
4	21.09 ±0.45	-2.52 ±0.70	3.66 ±0.58	-2.14 ±0.45	0.923	0.344	17.33	30.29	43.99	25.72	MeOH, BzOH, 2-ME, DCM, F, AcN, Acetone, NMP, EtOH
5	20.56 ±0.28	0.57 ±0.32	1.45 ±0.33	0.81 ±0.19	0.938	0.214	21.82	20.14	51.24	28.62	DMAc, DCM, 2-CE, DME, BzOH, Acetone, EtOH, AcN, 2-ME
6	17.45 ±0.76	6.69 ±0.90	-0.57 ±0.67	2.14 ±0.38	0.937	0.878	19.16	71.17	6.06	22.77	BzOH, 2-ME, 2-BuOH, F, DME, Toluene, DMAc, EtOH, DMF, DCM
7	22.03 ±0.49	2.79 ±0.64	0.64 ±0.37	2.11 ±0.34	0.945	0.278	22.04	50.36	11.55	38.09	2CE, DME, EtAc, 2-Pyr, BzOH, EtOH, F, DMSO, 2-ME, AcN
8	22.41 ±0.30	0.03 ±0.38	-1.77 ±0.27	1.98 ±0.21	0.950	0.246	36.80	0.79	46.83	52.38	2CE, DMSO, THF, BzOH, 2-Pyr, AcN
9	22.43 ±0.28	1.13 ±0.30	-0.64 ±0.27	0.97 ±0.16	0.916	0.200	13.98	41.24	23.36	35.40	DME, AcN, DMAc, 2ME, EtAc, 2-PrOH, ChO, NMP, MeOH DMSO
10	20.84 ±0.30	2.46 ±0.39	-1.57 ±0.25	2.12 ±0.21	0.946	0.214	33.83	40.00	25.53	34.47	2CE, BzOH, F, ChO, Toluene, 2-BuOH
11	20.80 ±0.43	2.56 ±0.46	-1.34 ±0.30	0.55 ±0.22	0.934	0.266	18.17	57.53	30.11	12.36	Toluene, iPrOH, EtOH, ChO, Acetone, BzOH, EtAc, DME, 2-Pyr, AcN
12	20.62 ±0.40	1.28 ±0.49	0.04 ±0.37	2.05 ±0.25	0.940	0.300	27.89	37.98	1.19	60.83	2CE, DME, BzOH, 2ME, AcN, DMSO, 2-BuOH
13	19.84 ±0.21	2.47 ±0.28	0.15 ±0.21	0.86 ±0.13	0.952	0.183	35.87	70.98	4.31	24.71	THF, BzOH, AcN, iPrOH, EtOH, Acetone, DCM
14	28.04 ±0.35	-3.86 ±0.44	-0.03 ±0.35	0.62 ±0.18	0.955	0.279	38.16	85.59	0.67	13.75	ChO, 2-BuOH, Toluene, ChO, iPrOH, EtOH, 2-Pyr
15	23.13 ±0.28	-0.33 ±0.29	-1.11 ±0.22	0.81 ±0.15	0.935	0.165	18.53	14.67	49.33	36.00	DCM, EtAc, THF, DME, ChO, iPrOH, 2CE, DMAc, Toluene
16	24.57 ±0.34	-1.25 ±0.32	-2.00 ±0.32	-0.88 ±0.15	0.946	0.188	28.63	30.27	48.43	21.31	Toluene, DMSO, DCM, BzOH, 2-ME, MeOH, EtAc, THF

^a Correlation coefficient; ^b Standard deviation; ^c Fisher test of significance; ^d The percentage contribution of solvatochromic parameters obtained by the use of Kamlet-Taft equation (%);

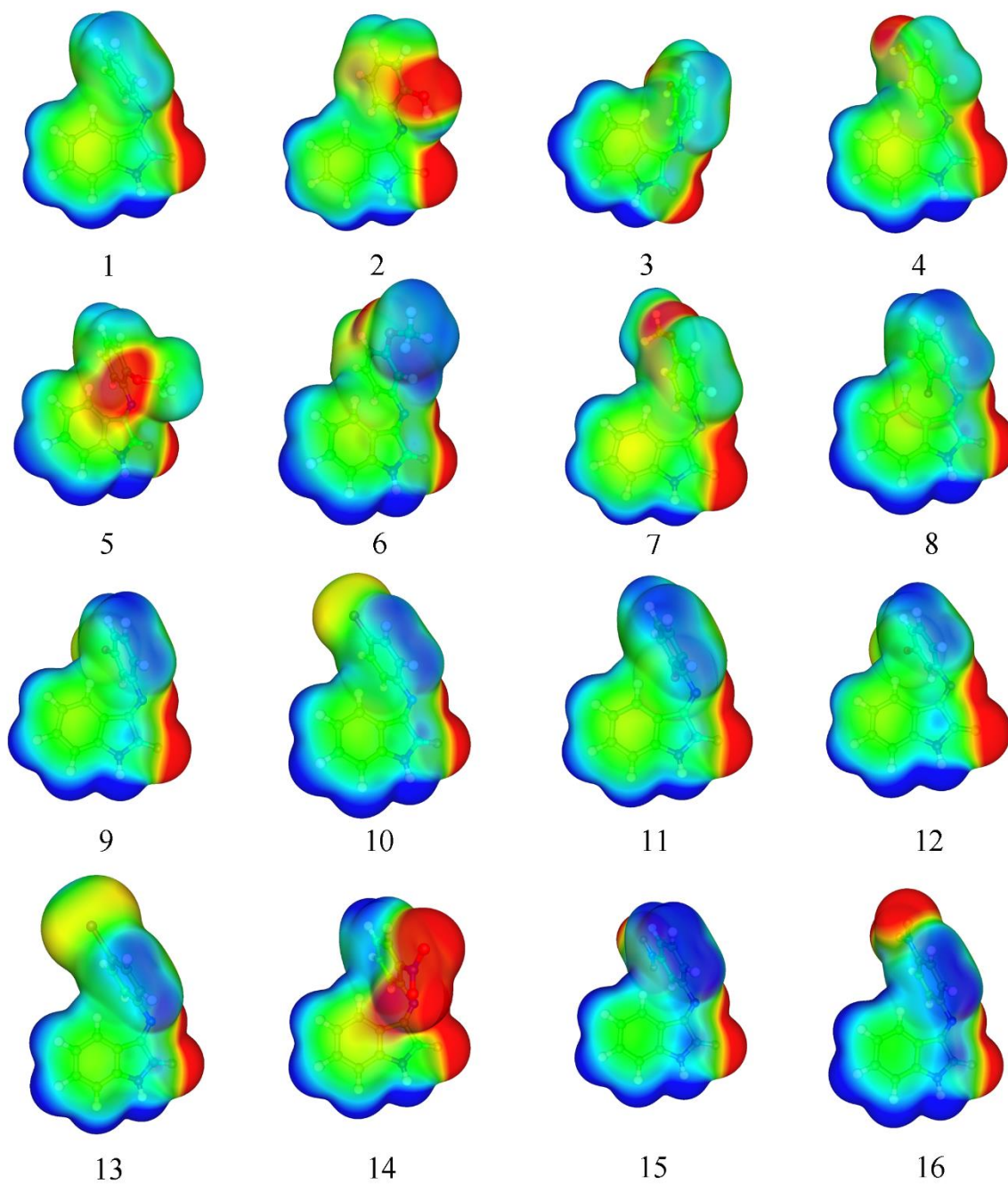


Figure S17. MEP map of compounds **1-16** in *E* form (gas phase) calculated by B3LYP/6-311G(d,p) method in ground state.

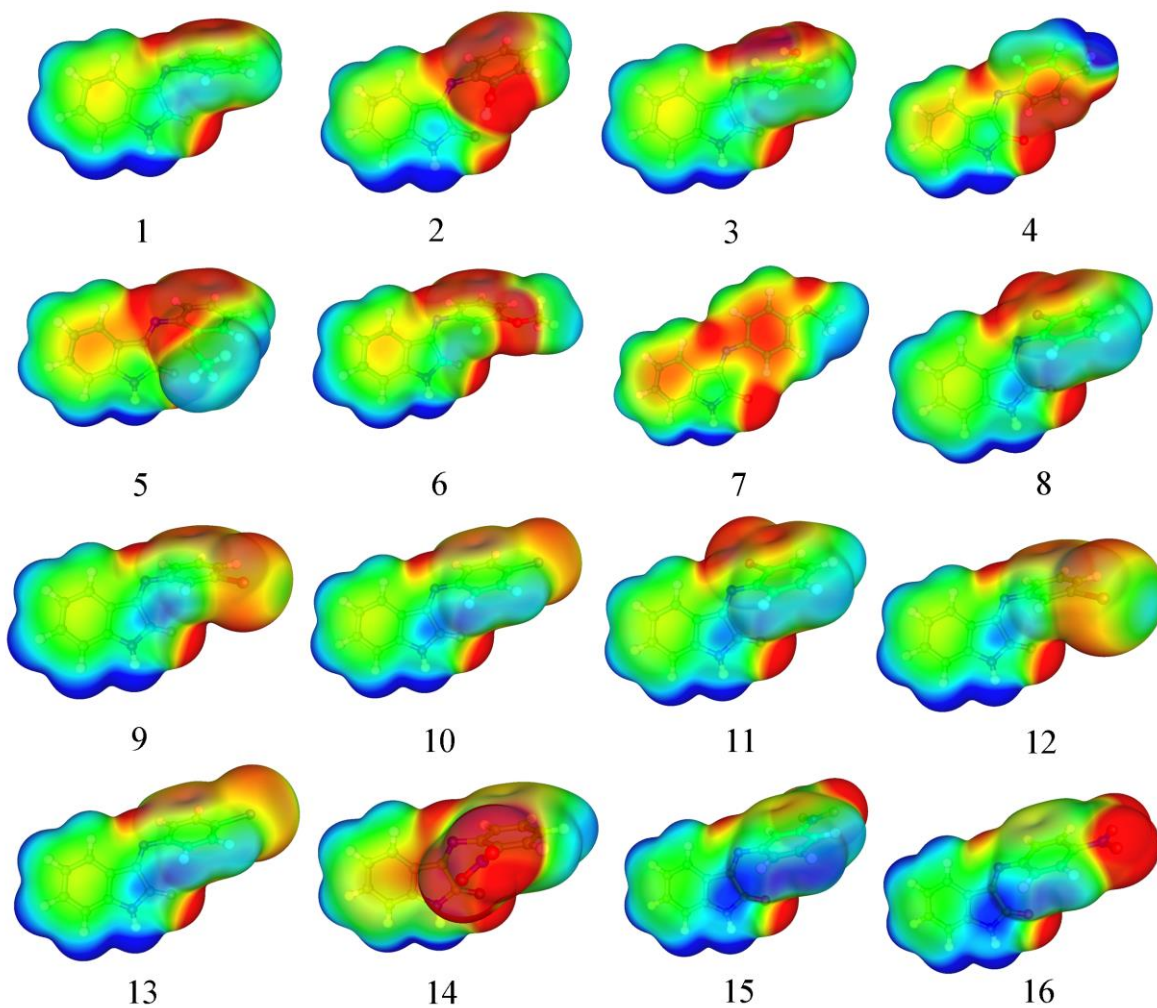


Figure S18. MEP map of compounds **1-16** in Z form (gas phase) calculated by B3LYP/6-311G(d,p) method in ground state in gas phase.

3.5. LFER analysis of UV data

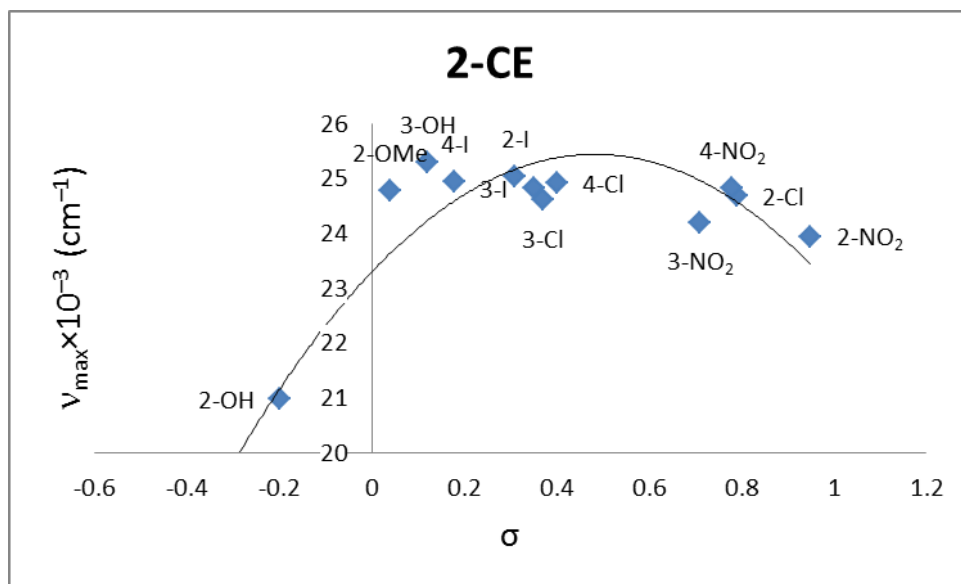


Figure S19. Correlation of the ν_{\max} vs substituent parameters for compounds **1-16** in 2-CE for *E* isomers.

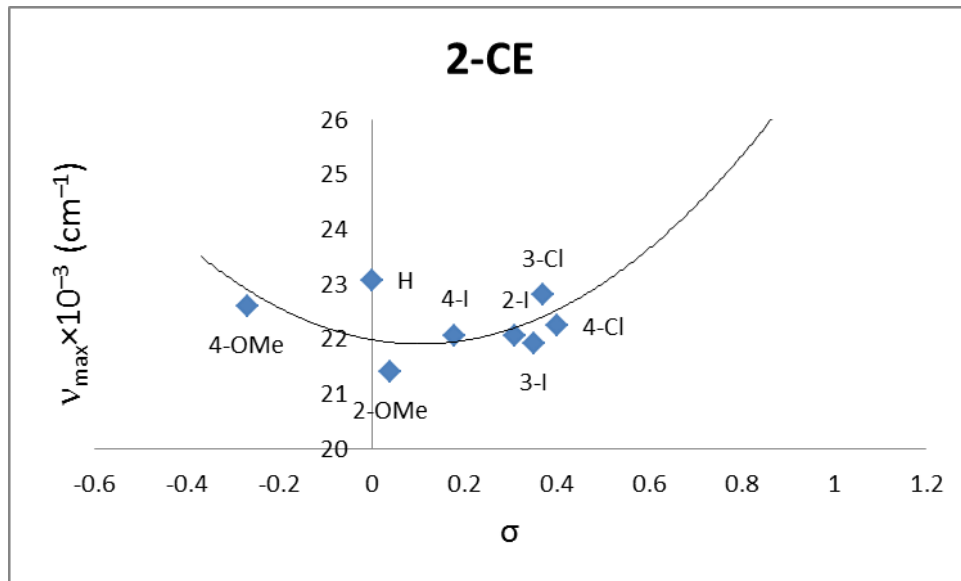


Figure S20. Correlation of the ν_{\max} vs substituent parameters for compounds **1-16** in 2-CE for *Z* isomers.

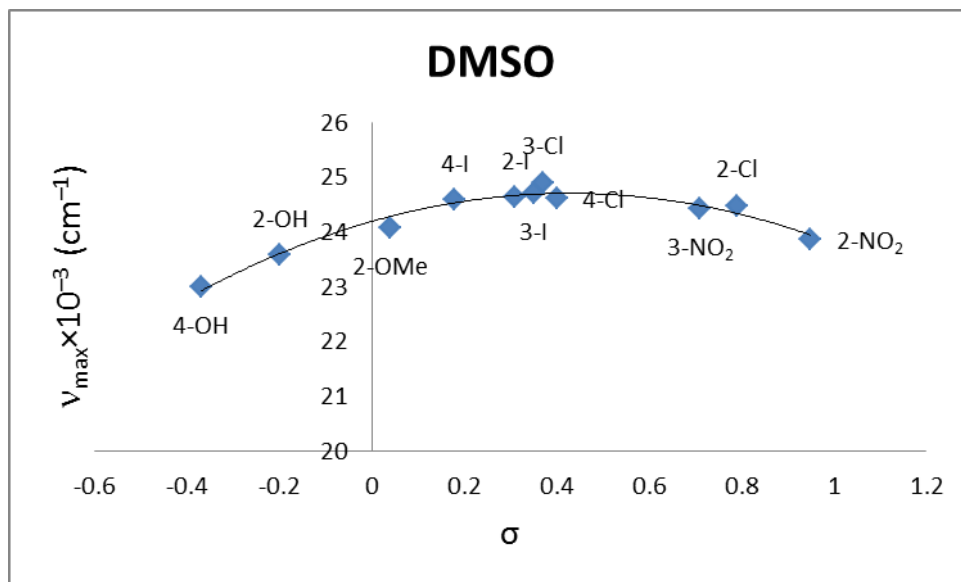


Figure S21. Correlation of the ν_{\max} vs substituent parameters for compounds **1-16** in DMSO for *E* isomers.

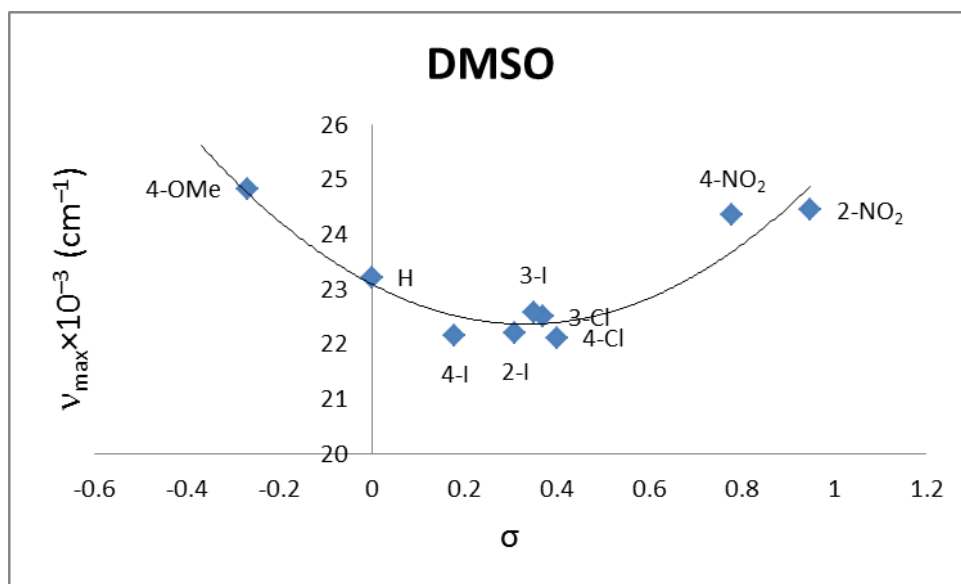


Figure S22. Correlation of the ν_{\max} vs substituent parameters for compounds **1-16** in DMSO for *Z* isomers.

3.6. LFER analysis of NMR data

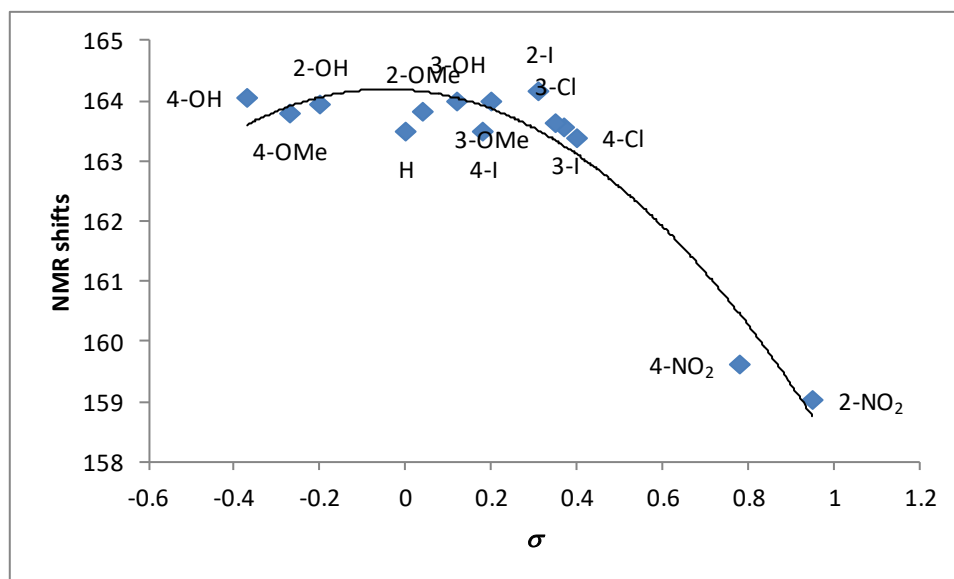


Figure S23. Correlation results of the *SCS* values of isatin derivatives (*E* isomers) with σ constants using Hammett Eq. (2) on C2; variable (σ^2) = -5.52, variable (σ) = -0.48, intercept = 164.18, $r = 0.964$.

3.7. Comparative LFER analysis of NMR for azomethine carbon of selected imino series

¹³C NMR chemical shifts of azomethine carbon have been investigated in order to study transmission of electronic effects of substituents in many organic compounds [14–19]. The literature values for chemical shifts of azomethine carbon are taken for *N*-benzylideneanilines (series **2**, Figure S19) [15], and *N*-(substituted phenyl)pyridine-2- and -3-aldimines (series **3**, and **4**, Figure S19) [16], *N*-(phenyl substituted)pyridine-4-aldimines (series **5**, Figure S20.) [17], and 4-substituted *N*-[1-(pyridine-3- and -4-yl)ethylidene]anilines (series **6** and **7**, Figure S20) [18].

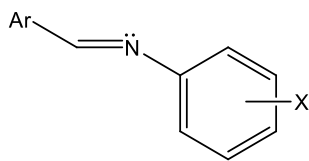


Figure S24. Structures of the 4-substituted *N*-benzylideneanilines (Ar = phenyl, series **2**), *N*-phenyl substituted aldimines (Ar = 3-pyridyl series **3**; Ar = 2-pyridyl series **4**; Ar = 4-pyridyl series **5**).

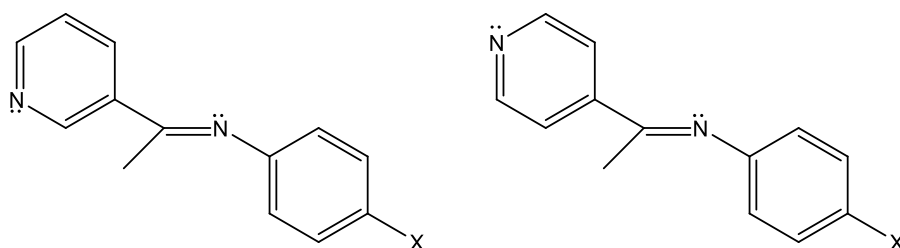


Figure S25. Structures of the 4-substituted *N*-[1-(pyridine-3-yl)ethylidene]anilines (series **6**) and 4-substituted *N*-[1-(pyridine-4-yl)ethylidene]anilines (series **7**).

To obtain a better insight into the transmission of electronic effects of the substituent X on the aniline ring, an extensive analysis of ^{13}C NMR chemical shifts of the carbon atoms of interest has been performed. The chemical shifts of the azomethine carbon atoms are given in Table S9 relative to the parent compounds.

Table S9. ^{13}C NMR chemical shifts of the azomethine carbon atoms in substituted *N*-benzylideneanilines (series **2**), *N*-(phenyl substituted)pyridine-3-aldimines (series **3**), *N*-(phenyl substituted)pyridine-2-aldimines (series **4**), *N*-(substituted phenyl)pyridine 4-aldimines (series **5**), *N*-[1-(pyridine-3-yl)ethylidene]anilines (series **6**) and *N*-[1-(pyridine-4-yl)ethylidene]anilines (series **7**).

X	series 2*	series 3	series 4	series 5	series 6	series 7
H	160.07	156.799	160.331	157.673	164.005	164.515
<i>p</i> - N(CH₃)₂	-4.45	-4.915	-5.097	-5.717	-1.475	-1.839
<i>p</i> - OH	-	-	-	-	-0.655	-0.819
<i>p</i> - OCH₃	-2.12	-2.021	-2.239	-2.676	-0.447	-0.237
<i>p</i> - CH₃	-1.26	-0.728	-0.691	-1.074	-0.054	-0.115
<i>p</i> - F	-0.47	-	-	-	-	0.856
<i>p</i> - Cl	0.33	0.701	0.492	0.492	0.933	1.056
<i>p</i> - Br	-	0.601	0.619	0.546	1.002	1.020
<i>p</i> - COOCH₃	-	-	1.857	1.785	-	2.185
<i>p</i> - COCH₃	-	1.857	1.857	1.930	1.368	2.185
<i>p</i> - COOEt	1.27	-	-	-	-	-
<i>p</i> - NO₂	-	2.39	3.023	-	-	-
<i>m</i> - NO₂	-	2.841	2.731	2.749	-	-
<i>m</i> - CF₃	-	1.548	1.621	1.493	-	-
<i>m</i> - Cl	-	-	0.947	-	-	-

* ^{13}C NMR chemical shifts (in ppm) expressed relative to the unsubstituted compound; downfield shifts are positive.

Hydroxy, methoxy, dimethylamino and methyl group as an electron-donor substituent induce downfield shifts on imino carbon, while electron donor substituent (halogen: chlorine and bromine, ester, acetyl, nitro and trifluoromethyl) induce upfield shifts. Fluorine atom induce downfield shifts on imino carbon in *N*-benzylideneanilines with the opposite effect in *N*-[1-(pyridine-4-yl)ethylidene]anilines.

From the literature data the chemical shifts of *N*-benzylideneanilines (series **2**) [15], and *N*-(substituted phenyl)pyridine-2-, and -3-aldimines (series **3** and **4**, respectively) [16], *N*-(phenyl substituted)pyridine-4-aldimines (series **5**) [17] and 4-substituted *N*-[1-(pyridine-3- and -4-yl)ethylidene]anilines (series **6** and **7**) [18], for azomethine carbon were correlated with different scales, the goodness of fit correlation were obtained with different

σ values, and the selection which is made is given in Table S2, and the obtained results are shown in Table 8.

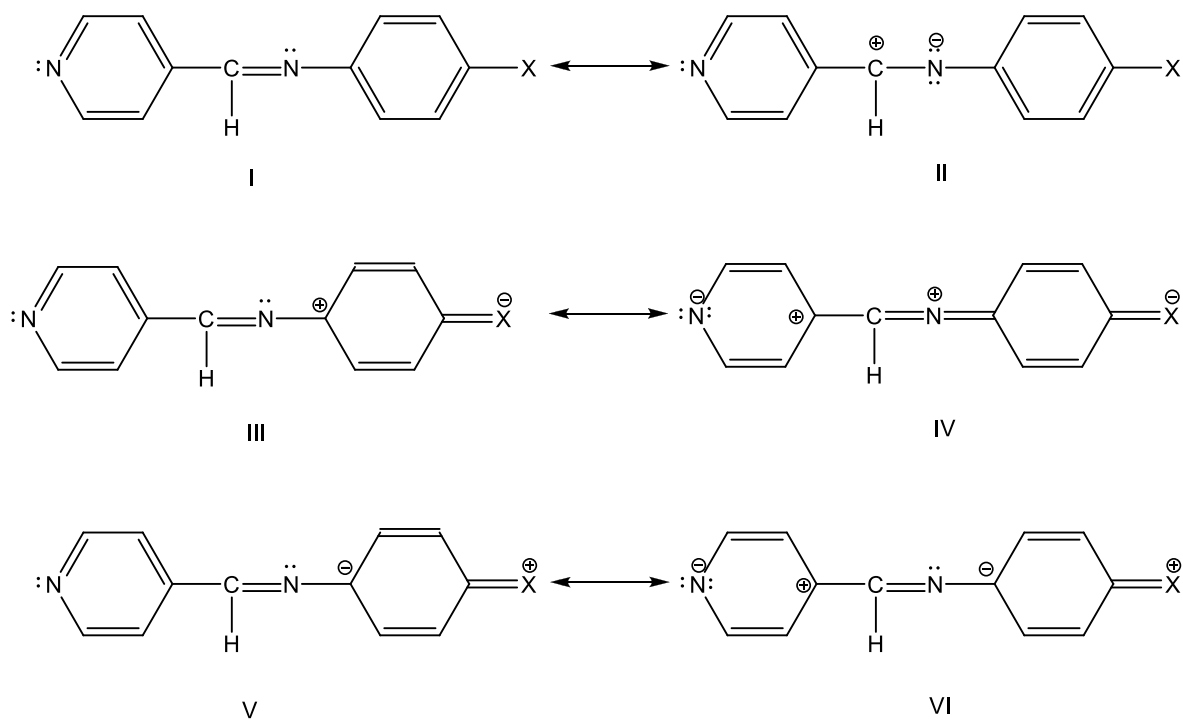


Figure S26. Mesomeric structures of imino derivatives with electron-donor and electron-acceptor group.

3.8. DFT, TD-DFT and Bader's analysis. Nature of the frontier molecular orbitals

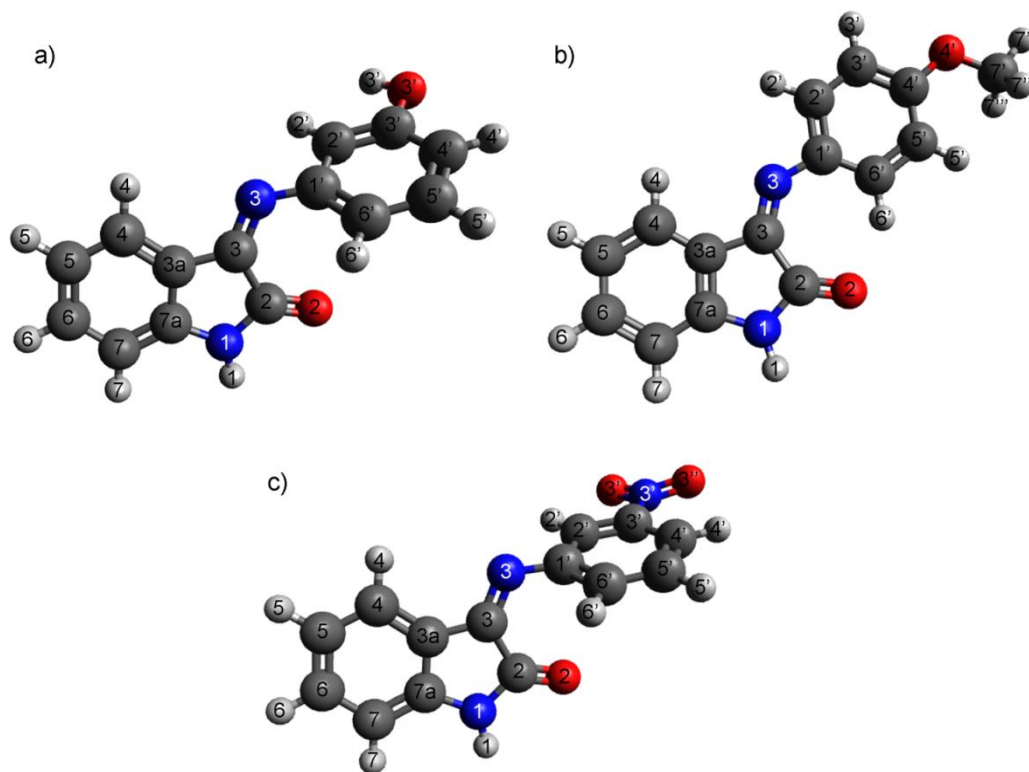


Figure S27. Numbering of the atoms used in Bader's analysis for all investigated compounds (examples given for a) **3** (3-OH), b) **6** (4-OMe) and c) **15** (3-NO₂) compounds).

Table S10. Elements of the optimized geometries of investigated compounds in Z form, obtained by MP2/6-31G(d,p) method.

Comp./Subst.	N1-C2	C2-C3	C3=N3	N3-Ph	θ
1 / H	1.3874	1.5418	1.2886	1.4107	57.191
2 / 2-OH	1.3705	1.5286	1.293	1.3919	48.46
3 / 3-OH	1.3877	1.5417	1.2885	1.4115	57.846
4 / 4-OH	1.3876	1.5405	1.2915	1.4051	50.287
5 / 2-OMe	1.3869	1.5362	1.2887	1.408	56.797
6 / 3-OMe	1.3877	1.5424	1.2875	1.4135	60.625
7 / 4-OMe	1.383	1.5409	1.2967	1.3924	0.01
8 / 2-Cl	1.3862	1.5399	1.2866	1.4102	67.495
9 / 3-Cl	1.3862	1.5421	1.288	1.4116	60.458
10 / 4-Cl	1.3861	1.5417	1.2893	1.4085	55.701
11 / 2-I	1.3845	1.5359	1.2916	1.4075	62.299
12 / 3-I	1.3846	1.5378	1.2919	1.4113	59.374
13 / 4-I	1.3844	1.5373	1.2927	1.4091	55.187
14 / 2-NO₂	1.3832	1.5343	1.2837	1.4146	82.077
15 / 3-NO₂	1.3847	1.5413	1.2867	1.4122	66.878
16 / 4-NO₂	1.3845	1.5412	1.2871	1.4111	63.527

Table S11. Results of TD-DFT calculations for transitions from ground to first vertical excited state for **Z** isomers in EtOH.

Compound No.	Energy (eV)	Oscillator strenght	Excitation	CI expansion coefficient*	% of single particle excitation contribution*
1	2.939	0.111	HOMO→LUMO	0.608	74
			HOMO-1→LUMO	0.212	9
			HOMO-4→LUMO	-0.200	8
2	2.999	0.245	HOMO→LUMO	0.592	70
			HOMO-3→LUMO	0.212	9
			HOMO-4→LUMO	0.200	8
			HOMO-2→LUMO	-0.158	5
3	2.922	0.11	HOMO→LUMO	0.608	74
			HOMO-4→LUMO	0.212	9
			HOMO-2→LUMO	-0.212	9
4	2.803	0.204	HOMO→LUMO	0.636	81
			HOMO-4→LUMO	-0.224	10
5	2.775	0.113	HOMO→LUMO	0.652	85
			HOMO-4→LUMO	0.158	5
			HOMO-3→LUMO	-0.141	4
6	2.939	0.093	HOMO→LUMO	0.548	60
			HOMO-2→LUMO	-0.292	17
			HOMO-4→LUMO	0.200	8
			HOMO-1→LUMO	0.187	7
7	3.181	0.528	HOMO→LUMO	0.663	88
			HOMO-1→LUMO	-0.212	9
8	3.004	0.064	HOMO→LUMO	0.587	69
			HOMO-1→LUMO	-0.265	14
			HOMO-4→LUMO	0.187	7
9	3.005	0.094	HOMO→LUMO	0.574	66
			HOMO-1→LUMO	-0.265	14
			HOMO-4→LUMO	0.200	8
			HOMO-3→LUMO	0.141	4
10	2.936	0.145	HOMO→LUMO	0.616	76
			HOMO-4→LUMO	-0.235	11
			HOMO-1→LUMO	0.158	5
			HOMO-2→LUMO	0.158	5
11	2.939	0.077	HOMO→LUMO	0.587	69
			HOMO-2→LUMO	-0.212	9
			HOMO-1→LUMO	-0.200	8
			HOMO-5→LUMO	0.187	7
12	2.97	0.099	HOMO→LUMO	0.566	64
			HOMO-2→LUMO	0.235	11
			HOMO-1→LUMO	-0.212	9
			HOMO-5→LUMO	0.173	6
13	2.92	0.166	HOMO→LUMO	0.604	73
			HOMO-4→LUMO	0.255	13

14	3.213	0.008	HOMO-1→LUMO	0.612	75
			HOMO→LUMO	-0.224	10
15	3.084	0.064	HOMO→LUMO	0.485	47
			HOMO-1→LUMO	-0.418	35
			HOMO-4→LUMO	0.173	6
16	3.073	0.127	HOMO→LUMO	0.490	48
			HOMO-1→LUMO	-0.381	29
			HOMO→LUMO+1	0.187	7

*Results are shown only for excitations with contribution greater than 10%

Table S12. Results of TD-DFT calculations for transitions from ground to first vertical excited state for *E* isomers in EtOH.

Compound No.	Energy (eV)	Oscillator strength	Excitation	CI expansion coefficient*	% of single particle excitation contribution*
1	3.501	0.074	HOMO→LUMO	0.700	98
2	3.023	0.296	HOMO→LUMO	0.667	89
3	3.376	0.025	HOMO→LUMO	0.570	65
			HOMO-2→LUMO	0.316	20
			HOMO-4→LUMO	0.187	7
			HOMO-5→LUMO	-0.158	5
4	3.087	0.093	HOMO→LUMO	0.656	86
			HOMO-4→LUMO	0.173	6
			HOMO-5→LUMO	0.158	5
5	3.237	0.087	HOMO→LUMO	0.574	66
			HOMO-1→LUMO	-0.324	21
			HOMO-4→LUMO	0.158	5
6	3.361	0.006	HOMO→LUMO	0.561	63
			HOMO-2→LUMO	0.324	21
			HOMO-4→LUMO	-0.187	7
			HOMO-5→LUMO	-0.158	5
7	3.073	0.11	HOMO→LUMO	0.656	86
			HOMO-4→LUMO	0.173	6
			HOMO-5→LUMO	-0.158	5
8	3.402	0.026	HOMO-1→LUMO	0.543	59
			HOMO→LUMO	-0.354	25
			HOMO-4→LUMO	0.173	6
9	3.447	0.07	HOMO→LUMO	0.640	82
			HOMO-1→LUMO	0.235	11
10	3.469	0.079	HOMO→LUMO	0.704	99
11	3.318	0.022	HOMO→LUMO	0.447	40
			HOMO-1→LUMO	0.424	36
			HOMO-2→LUMO	-0.255	13
			HOMO-4→LUMO	0.158	5
12	3.4	0.082	HOMO→LUMO	0.612	75
			HOMO-1→LUMO	-0.200	8
			HOMO-2→LUMO	0.200	8
13	3.458	0.085	HOMO-1→LUMO	0.700	98
14	3.383	0.08	HOMO→LUMO	0.678	92
15	3.414	0.084	HOMO→LUMO+1	0.616	76
			HOMO→LUMO	-0.308	19
16	3.411	0.095	HOMO→LUMO	0.696	97

*Results are shown only for excitations with contribution greater than 10%

Table S13. Calculated energies of the HOMO and LUMO orbitals and energy gap for compounds **1 - 16** in gas phase.

Compound	Isomer	Gas phase		
		Orbitals energy (eV)		
		E_{HOMO}	E_{LUMO}	E_{gap}
1	<i>Z</i>	-7.36	-1.42	5.94
	<i>E</i>	-7.85	-1.32	6.53
2	<i>Z</i>	-7.44	-1.68	5.76
	<i>E</i>	-7.35	-1.71	5.64
3	<i>Z</i>	-7.20	-1.46	5.74
	<i>E</i>	-7.62	-1.37	6.25
4	<i>Z</i>	-6.96	-1.37	5.59
	<i>E</i>	-7.28	-1.33	5.95
5	<i>Z</i>	-6.99	-1.29	5.70
	<i>E</i>	-7.63	-1.37	6.26
6	<i>Z</i>	-7.27	-1.35	5.93
	<i>E</i>	-7.51	-1.32	6.18
7	<i>Z</i>	-7.03	-1.43	5.60
	<i>E</i>	-7.19	-1.30	5.89
8	<i>Z</i>	-7.54	-1.51	6.04
	<i>E</i>	-7.92	-1.45	6.48
9	<i>Z</i>	-7.61	-1.59	6.02
	<i>E</i>	-7.99	-1.49	6.49
10	<i>Z</i>	-7.43	-1.61	5.82
	<i>E</i>	-7.88	-1.49	6.39
11	<i>Z</i>	-7.51	-1.61	5.90
	<i>E</i>	-7.84	-1.48	6.36
12	<i>Z</i>	-7.59	-1.64	5.95
	<i>E</i>	-7.93	-1.52	6.41
13	<i>Z</i>	-7.39	-1.67	5.72
	<i>E</i>	-7.75	-1.51	6.24
14	<i>Z</i>	-7.91	-1.51	6.40
	<i>E</i>	-8.00	-1.57	6.43
15	<i>Z</i>	-7.93	-1.75	6.18
	<i>E</i>	-8.14	-1.72	6.42
16	<i>Z</i>	-7.99	-1.91	6.08
	<i>E</i>	-8.21	-1.76	6.46

Table S14. Calculated energies of the HOMO and LUMO orbitals and energy gap for compounds **1 - 16** in DMSO, EtOH and AcN.

Comp.	Isomer	DMSO			EtOH			AcN		
		E_{HOMO}	E_{LUMO}	E_{gap}	E_{HOMO}	E_{LUMO}	E_{gap}	E_{HOMO}	E_{LUMO}	E_{gap}
1	Z	-7.58	-1.57	6.01	-7.57	-1.56	6.00	-7.57	-1.57	6.00
	E	-7.86	-1.45	6.41	-7.86	-1.45	6.42	-7.86	-1.45	6.41
2	Z	-7.65	-1.80	5.86	-7.65	-1.79	5.85	-7.65	-1.80	5.85
	E	-7.47	-1.76	5.71	-7.46	-1.76	5.70	-7.46	-1.76	5.71
3	Z	-7.46	-1.59	5.88	-7.45	-1.58	5.87	-7.46	-1.59	5.87
	E	-7.74	-1.48	6.27	-7.74	-1.47	6.26	-7.74	-1.47	6.26
4	Z	-7.19	-1.55	5.64	-7.18	-1.54	5.64	-7.19	-1.55	5.64
	E	-7.39	-1.46	5.93	-7.39	-1.46	5.93	-7.39	-1.46	5.93
5	Z	-7.30	-1.52	5.78	-7.29	-1.51	5.78	-7.30	-1.52	5.78
	E	-7.76	-1.55	6.21	-7.76	-1.54	6.21	-7.76	-1.55	6.21
6	Z	-7.58	-1.55	6.03	-7.57	-1.54	6.03	-7.58	-1.54	6.03
	E	-7.67	-1.46	6.21	-7.67	-1.46	6.21	-7.67	-1.46	6.21
7	Z	-7.23	-1.64	5.59	-7.22	-1.63	5.59	-7.22	-1.64	5.59
	E	-7.35	-1.47	5.88	-7.34	-1.46	5.88	-7.34	-1.46	5.88
8	Z	-7.74	-1.62	6.12	-7.73	-1.61	6.12	-7.74	-1.61	6.12
	E	-7.91	-1.57	6.34	-7.91	-1.57	6.34	-7.91	-1.57	6.34
9	Z	-7.72	-1.64	6.08	-7.71	-1.64	6.08	-7.72	-1.64	6.08
	E	-7.90	-1.53	6.37	-7.90	-1.53	6.37	-7.90	-1.53	6.37
10	Z	-7.58	-1.66	5.93	-7.58	-1.65	5.92	-7.58	-1.66	5.93
	E	-7.90	-1.51	6.38	-7.90	-1.51	6.39	-7.90	-1.51	6.38
11	Z	-7.71	-1.71	6.00	-7.70	-1.70	6.00	-7.70	-1.70	6.00
	E	-7.91	-1.60	6.31	-7.91	-1.59	6.32	-7.91	-1.60	6.31
12	Z	-7.71	-1.69	6.03	-7.71	-1.68	6.03	-7.71	-1.69	6.03
	E	-7.88	-1.56	6.32	-7.89	-1.56	6.33	-7.88	-1.56	6.32
13	Z	-7.56	-1.71	5.85	-7.55	-1.70	5.85	-7.56	-1.71	5.85
	E	-7.85	-1.53	6.32	-7.85	-1.53	6.32	-7.85	-1.53	6.32
14	Z	-7.91	-1.59	6.33	-7.91	-1.58	6.33	-7.91	-1.59	6.33
	E	-7.93	-1.63	6.30	-7.93	-1.63	6.30	-7.93	-1.63	6.30
15	Z	-7.84	-1.66	6.18	-7.84	-1.66	6.19	-7.84	-1.66	6.18
	E	-7.93	-1.74	6.19	-7.94	-1.73	6.20	-7.93	-1.73	6.20
16	Z	-7.86	-1.87	5.99	-7.86	-1.87	5.99	-7.86	-1.87	5.99
	E	-7.95	-1.61	6.33	-7.96	-1.62	6.34	-7.95	-1.62	6.34

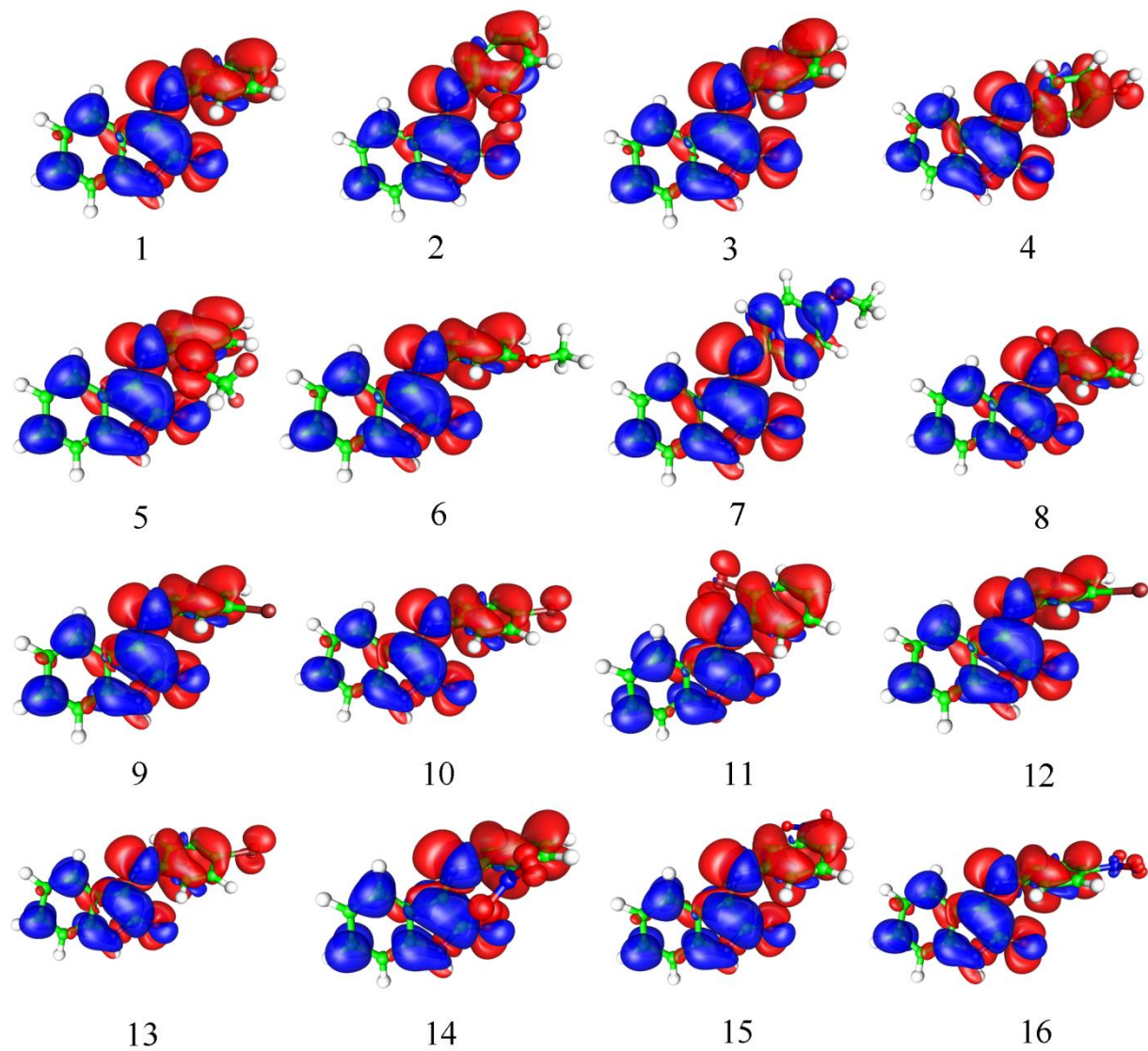


Figure S28. ICT processes from ground state (red) to excited state (blue) of compounds **1-16** for Z isomers.

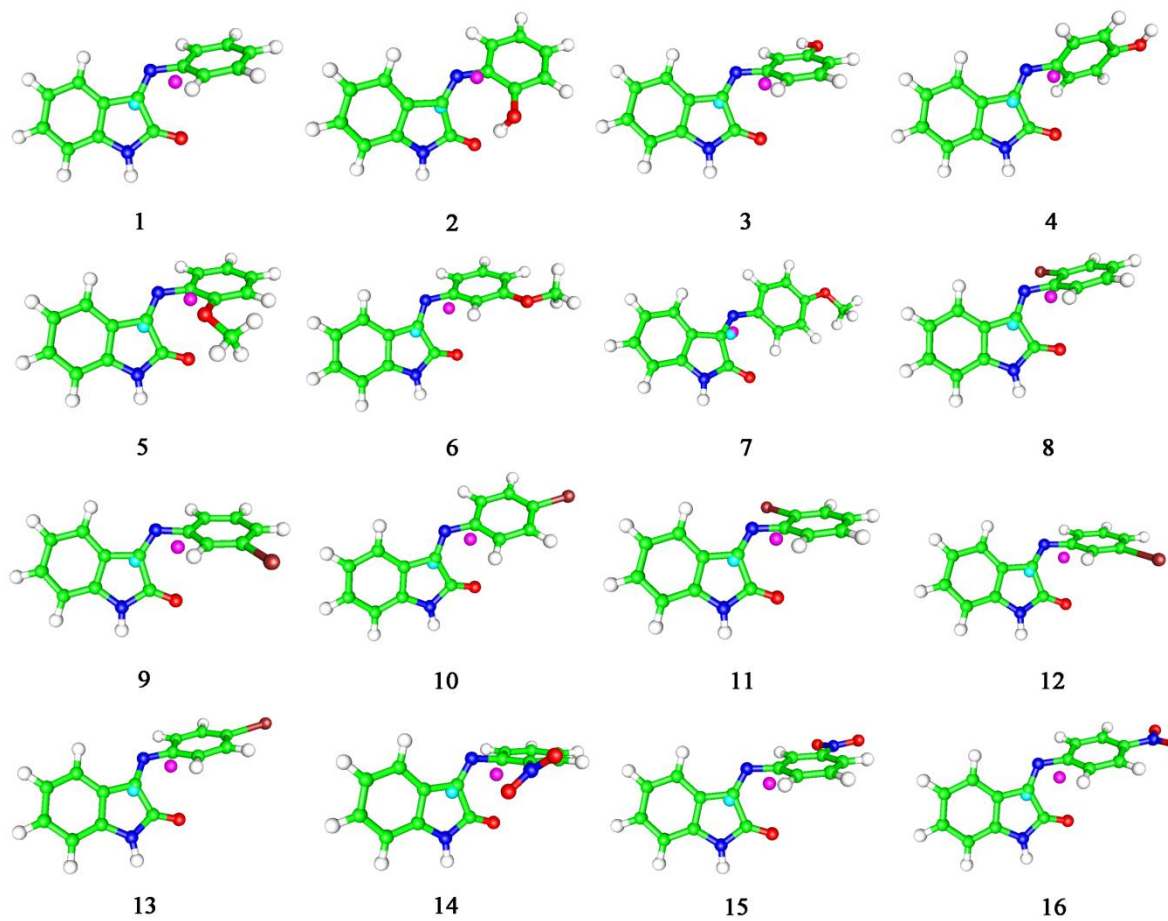


Figure S29. ICT in compounds **1-16** for *Z* isomers. Positions of barycenters for charge loss (cyan circle) and charge gain (violet circle) upon transition.

Table S15. Difference in atomic charges (Δ_{Charge}) between excited and ground state of appropriate atom in *Z* and *E* isomers.

Atom number /substituent Isomer	Δ_{Charge}													
	H		2-OH		3-OH		4-OH		2-OMe		3-OMe		4-OMe	
	Z	E	Z	E	Z	E	Z	E	Z	E	Z	E	Z	E
C2	0.0442	0.0494	0.0533	0.0341	0.0496	0.0494	0.047	0.0472	0.0579	0.0447	0.0445	0.0508	-0.0445	0.0477
C3	0.1473	0.1557	0.1137	0.1577	0.1523	0.1683	0.1406	0.1866	0.1596	0.1647	0.1504	0.1742	0.0676	0.1862
C3a	-0.0024	-0.0038	-0.0017	-0.0028	-0.0019	-0.0034	-0.0021	-0.0014	-0.0003	-0.0052	-0.0021	-0.0019	-0.0094	-0.0011
C4	0.0217	0.0128	0.0089	0.0332	0.0243	0.0124	0.0199	0.0106	0.0272	0.0094	0.0235	0.0133	-0.0073	0.0114
C5	-0.0001	-0.0004	0	-0.0006	-0.0001	-0.0002	-0.0001	-0.0002	0	-0.0002	-0.0001	-0.0003	0	-0.0002
C6	0.037	0.0618	0.0298	0.0342	0.0383	0.0602	0.0331	0.0507	0.0401	0.0517	0.0394	0.0605	0.033	0.0424
C7	0	-0.0001	0	0.0001	0	-0.0001	0	0.0001	0	-0.0001	0	0	0	0.0001
C7a	0.0346	0.051	0.0304	0.0242	0.0356	0.051	0.0309	0.0482	0.0364	0.0422	0.0367	0.0523	0.0296	0.0478
C1'	-0.0013	-0.0031	-0.0167	-0.0096	-0.001	-0.0023	-0.0098	-0.0023	-0.0011	-0.0022	-0.0007	-0.004	-0.0037	-0.0019
C2'	-0.0177	-0.0335	-0.0376	-0.0861	-0.0539	-0.0229	-0.0663	-0.0972	-0.0617	-0.0504	-0.0823	-0.0334	0.0013	-0.0693
C3'	-0.0455	-0.0456	-0.0443	-0.0191	-0.0046	-0.0412	-0.0064	-0.0104	-0.035	-0.0231	-0.0022	-0.0493	0	-0.0393
C4'	-0.0155	-0.0168	-0.0108	-0.0208	-0.0188	-0.0225	-0.0127	-0.0183	-0.0233	-0.0206	-0.0149	-0.0247	0.0387	-0.0191
C5'	-0.0081	-0.0583	-0.0186	-0.0106	-0.043	-0.0551	-0.0045	-0.0656	-0.0091	-0.0411	-0.0438	-0.0618	0	-0.0621
C6'	-0.0548	-0.0359	-0.0435	-0.0629	-0.0539	-0.0487	-0.0601	-0.0277	-0.0774	-0.0385	-0.0188	-0.0491	-0.0113	-0.0261
C7' (OCH₃)									-0.0182	-0.0048	-0.0059	-0.0011	0	-0.0068
H1	0	0	0	-0.0002	-0.0001	-0.0006	-0.0002	0	0	0	-0.0008	-0.0002	0	-0.0001
H4	0	0	0	0	0	-0.0036	0	-0.0015	0	0	0	-0.0022	0	-0.0025
H5	-0.0001	0	-0.0009	-0.0005	0	-0.0034	0	-0.0017	-0.0001	0	0	0	-0.0021	-0.0001
H6	0	-0.0009	0	0	0	0	0	0	0	0	0	-0.0003	0	0
H7	0	0	0	0	0	-0.0004	0	-0.0001	0	-0.0004	-0.0002	0	0	-0.0002
H2'	0	0	-	-	0	0	0	0	-	-	0	0	0	-0.0007
H3'	-0.0101	-0.0261	0	-0.0006	-	-	-0.0101	-0.0208	-0.0095	-0.0085	-	-	0	-0.0096
H4'	-0.0158	-0.0143	-0.0085	-0.0157	0	-0.0251	-	-	-0.0089	-0.0208	-0.014	-0.0294	-	-
H5'	-0.0209	-0.0247	0	-0.0151	-0.0099	-0.0485	-0.0064	-0.0169	-0.0133	-0.0205	-0.01	-0.0299	-0.0001	-0.0184
H6'	0	0	0	0	0	0	-0.0216	0	-0.0002	0	-0.0001	-0.0027	0	-0.0009
H (OH)			-0.0118	0	-0.0037	-0.0007	-0.0066	-0.0129						
H' (OCH₃)									-0.0007	-0.0003	-0.0012	-0.0011	0	-0.0053
H'' (OCH₃)									0	-0.0019	-0.0004	-0.0038	0.0001	-0.0009
H''' (OCH₃)									0	0	-0.0001	-0.0014	0.0002	-0.0032
O2	-0.0385	0.0453	0.0324	0.0253	-0.0407	0.0453	-0.0021	0.0452	-0.0224	0.0368	-0.0404	0.0479	-0.0312	0.0446
O (OH)			-0.0101	-0.0332	-0.0234	-0.0268	-0.0378	-0.0577						
O (OCH₃)									-0.0191	-0.0285	-0.0045	-0.0266	0.011	-0.0618
N1	-0.0048	0.0048	0.0127	-0.0006	-0.0042	0.0043	-0.0012	0.0044	0.0029	0.0022	-0.0053	0.0056	-0.0098	0.0043
N3	-0.0385	-0.1171	-0.0768	-0.0303	-0.021	-0.0855	-0.0234	-0.0586	-0.0236	-0.0848	-0.0467	-0.0813	-0.0622	-0.0551

Table S16. Difference in atomic charges (Δ_{Charge}) between excited and ground state of appropriate atom in *Z* and *E* isomers.

Atom number / supstituent Isomer	Δ_{Charge}											
	2-Cl		3-Cl		4-Cl		2-I		3-I		4-I	
	Z	E	Z	E	Z	E	Z	E	Z	E	Z	E
C2	0.047	0.0487	0.04	0.0472	0.0425	0.0489	0.0496	0.0491	0.0448	0.0445	0.0451	0.0498
C3	0.1631	0.1631	0.1492	0.1451	0.1495	0.1795	0.1522	0.1712	0.1455	0.1567	0.1481	0.1547
C3a	-0.0017	-0.0049	-0.0029	-0.0058	-0.0029	-0.0036	-0.002	-0.0045	-0.0027	-0.0065	-0.0027	-0.0037
C4	0.0273	0.014	0.0225	0.0157	0.0201	0.0162	0.0219	0.0159	0.021	0.0045	0.0198	0.019
C5	-0.0001	-0.0004	-0.0001	-0.0003	-0.0002	-0.0004	-0.0001	-0.0004	-0.0001	-0.0003	-0.0002	-0.0004
C6	0.0434	0.0612	0.0382	0.0543	0.0357	0.038	0.0407	0.0608	0.0373	0.0255	0.0353	0.0589
C7	0	-0.0002	0	-0.0001	0	-0.0001	0	-0.0001	0	-0.0002	0	-0.0001
C7a	0.0408	0.0502	0.0349	0.0485	0.0326	0.0518	0.038	0.0498	0.0335	0.0444	0.0333	0.0518
C1'	-0.0004	-0.0018	-0.0007	-0.001	-0.0007	-0.0013	-0.0013	-0.0012	-0.0013	-0.0009	-0.0006	0
C2'	-0.0394	-0.0508	-0.0693	-0.044	-0.0359	-0.0335	-0.033	-0.0374	-0.066	-0.0521	-0.0288	-0.0342
C3'	-0.0421	-0.0441	-0.0014	-0.0302	-0.027	-0.0483	-0.0434	-0.0489	-0.0011	-0.0249	-0.0253	-0.0451
C4'	-0.0163	-0.0138	-0.0171	-0.0162	-0.0139	-0.0176	-0.0174	-0.0119	-0.015	-0.0098	-0.0246	-0.026
C5'	-0.0269	-0.0433	-0.0437	-0.0547	-0.0156	-0.0524	-0.0187	-0.0486	-0.0414	-0.043	-0.0231	-0.0449
C6'	-0.0562	-0.0293	-0.0192	-0.0318	-0.0467	-0.0336	-0.0542	-0.0319	-0.0181	-0.0277	-0.0505	-0.0329
H1	0	-0.0007	0	-0.0005	0	-0.0034	-0.0038	-0.0006	0	-0.0005	-0.0004	-0.0046
H4	0	0	0	-0.0008	0	-0.0075	-0.0036	-0.0025	0	-0.0003	0	-0.0026
H5	0	-0.0073	-0.0002	-0.0008	0	0	-0.0005	-0.0013	-0.0001	0	-0.0003	0
H6	-0.0013	-0.0001	0	-0.0011	0	-0.0003	0	-0.0002	0	-0.0002	-0.0003	0
H7	0	-0.0014	-0.0002	-0.0004	0	-0.0008	0	-0.0002	-0.0001	-0.0012	-0.0002	-0.0069
H2'	-	-	0	-0.0002	0	-0.0009	-	-	0	0	0	0
H3'	-0.0122	-0.0232	-	-	-0.0083	-0.0247	-0.0077	-0.0225	-	-	-0.007	-0.0285
H4'	-0.016	-0.016	-0.0147	-0.019	-	-	-0.0183	-0.0149	-0.0108	-0.0133	-	-
H5'	-0.0299	-0.0249	-0.0086	-0.0126	-0.0063	-0.0233	-0.0135	-0.027	-0.0001	-0.0108	-0.0018	-0.0276
H6'	0	0	0	-0.0044	0	-0.0008	0	-0.0005	0	-0.0001	-0.0233	-0.0011
O2	-0.0338	0.0422	-0.043	0.0364	-0.0372	0.0433	-0.0345	0.0225	-0.0471	0.0342	-0.015	0.0428
N1	-0.004	0.0043	-0.007	0.0025	-0.0049	0.005	-0.0029	0.0037	-0.0044	-0.0012	-0.0029	0.0049
N3	-0.0232	-0.103	-0.0436	-0.1035	-0.0433	-0.0941	-0.0221	-0.0715	-0.0426	-0.0842	-0.0421	-0.095
Cl	-0.0181	-0.0185	-0.013	-0.0223	-0.0376	-0.036						
I							-0.0254	-0.0473	-0.0214	-0.0329	-0.0325	-0.0284

Table S17. Difference in atomic charges (Δ_{Charge}) between excited and ground state of appropriate atom in *Z* and *E* isomers.

Atom number / substituent Isomer	Δ_{Charge}					
	14 (2-NO ₂)		15 (3-NO ₂)		16 (4-NO ₂)	
	<i>Z</i>	<i>E</i>	<i>Z</i>	<i>E</i>	<i>Z</i>	<i>E</i>
C2	0.0402	0.0272	0.0426	0.0405	0.0362	0.0414
C3	0.1695	0.1401	0.1528	0.1492	0.1511	0.1393
C3a	-0.0016	-0.0104	-0.0031	-0.0088	-0.0032	-0.0082
C4	0.0327	0.0089	0.0247	0.0078	0.0215	0.0195
C5	0	-0.0015	-0.0001	-0.0005	-0.0002	-0.0005
C6	0.0496	0.0303	0.0406	0.0253	0.0368	0.0223
C7	-0.0001	-0.0005	0	-0.0003	0	-0.0004
C7a	0.0481	-0.0121	0.0375	0.0391	0.0329	0.0475
C1'	-0.001	-0.0003	0	-0.0018	-0.0002	-0.0013
C2'	-0.0418	-0.025	-0.022	-0.0325	-0.0167	-0.0247
C3'	-0.0324	-0.0163	-0.0438	-0.0286	-0.0374	-0.0316
C4'	-0.0131	-0.0068	-0.0144	-0.0129	-0.0125	-0.0154
C5'	-0.0386	-0.0304	-0.031	-0.0299	-0.0319	-0.0314
C6'	-0.0267	-0.0181	-0.036	-0.0223	-0.0347	-0.0238
H1	0	-0.005	-0.0017	-0.0001	0	-0.0004
H4	0	-0.0012	0	-0.0023	0	0
H5	-0.0003	-0.0016	0	0	0	-0.0022
H6	-0.0002	-0.0012	0	0	-0.0001	-0.0001
H7	-0.0008	-0.0026	0	-0.0009	0	-0.002
H2'	-	-	0	0	0	0
H3'	-0.0159	-0.0139	-	-	-0.006	-0.0156
H4'	-0.0162	-0.0107	0	-0.0101	-	-
H5'	-0.0188	-0.0189	-0.0106	-0.0143	-0.0045	-0.0161
H6'	0	-0.0001	0	-0.0001	-0.0009	-0.0001
O2	-0.0526	0.0028	-0.0486	0.0207	-0.0504	0.0166
O' (NO₂)	-0.0055	-0.0019	-0.0019	-0.0007	-0.0023	-0.0061
O'' (NO₂)	-0.0054	-0.0013	-0.0098	-0.014	-0.0034	-0.0056
N1	-0.0056	-0.0076	-0.0074	-0.0058	-0.0099	0.0004
N3	-0.0599	-0.018	-0.0515	-0.0837	-0.0528	-0.0852
N (NO₂)	-0.0037	-0.0038	-0.0035	-0.0129	-0.0114	-0.0163

3.8.1. Detail analysis of difference in atomic charges (Δ_{Charge}) between excited and ground state of appropriate atom in *Z* and *E* isomers

***E* isomer:** ICT mechanism of *E* isomers indicate that processes of the electron density mainly decrease on isatin heterocyclic ring take place in the course of the transition from ground to excited state. The opposite is true for the substituted phenyl ring. According to the trend of ICT processes, the investigated compounds can be divided into three groups: the first one includes unsubstituted compound and ones with hydroxy and methoxy group, *i.e.* compounds **1–7**, the second with halogen substituents, *i.e.* compounds **8–13**, and the third ones nitro substituted compounds **14–16** (Figs. 5 and Tables S15-S17).

In the first group, hydroxy and methoxy group exert moderate to strong electron-donating effects, respectively, causing reduction of the amount of charge (Δ_{charge}) in the phenyl ring. If hydroxy and methoxy groups are in *ortho* position the electron density on C2', C4' and C6' showed increasing trend in comparison to compound **1** (Table S15) from ground to excited states. The most prominent change of the amount of charge (Δ_{charge}) on C2' between the compounds **1** and **2** (2-OH), -0.0335 and -0.0861 , and C6', -0.0335 and -0.0629 , respectively, exhibited hydroxy substituted compounds in *ortho* position. It is well known that the *ortho* effect consists of polar effects (inductive and resonance), transmitted mainly through π -resonance system, and of pure steric effects, transmitted through space. The electrostatic interactions and hydrogen bonding effect cause more significant shift of electronic densities to electron-deficient local environment through space. The *ortho* hydroxy substituted isatin derivative showed lose on C1' from -0.0031 (**1**) to -0.0096 (**2**, 2-OH).

Also, the presence of hydroxy and methoxy in *meta*-position cause the increase of the electron density on C4' and C6' carbons. The largest increase was noted on C6'. The values of -0.0359 (**1**) to -0.0487 **3** (3-OH) and -0.0491 **6** (3-OMe) were found, respectively. The electron-donating effect of 4-OH and 4-OMe substituent cause higher increase of electron density at C2', from -0.0335 (**1**) to -0.0972 and -0.0693 found for comps. **4** (4-OH) and **7** (4-OMe), respectively. In all hydroxy and methoxy substituted molecules, Δ_{charge} in isatin ring have similar values on C2, C3, O2 (C2=O) and N1 atom. Additionally, the hydroxy and methoxy groups in *ortho* position cause an increase of the electron density at O2 (C2=O), from 0.0453 (**1**) to 0.0253 and 0.0368 found for comps. **2** (2-OH) and **5** (2-OMe),

respectively. Small increase of electron density was found on N1, from 0.0048 (**1**) to -0.0006 (**2**, 2-OH) and 0.0022 (**5**, 2-OMe). The opposite trend was found for N3 imino nitrogen (C=N), where significant changes of Δ_{charge} , in comparison to comp. **1** (-0.1171), were found: -0.0303, -0.0586 and -0.0551 for comps. **2** (2-OH), **4** (4-OH) and **7** (4-OMe), respectively.

The second group showed similar ICT process to those observed in the first group. The electron density was mainly populated on the phenyl ring in excited state, while the decreasing trend was noted in isatin ring. The presence of a halogen substituent cause increase electron density on C2' in compound **8** (2-Cl), from -0.0335 (**1**) to -0.0508, -0.044 (**9**; 3-Cl) and -0.0521 (**12**; 3-I) (Table S16) from ground to excited state. In a similar manner halogen substituents cause negligible, at C1', and moderate decrease electron density at C3': from -0.0456 (**1**) to -0.0302 (**9**; 3-Cl) and -0.0249 (**12**; 3-I). Generally, in these groups the Δ_{charge} values are similar for C2, C3, O2 (C2=O) and N1 atoms. Highest value for C3, 0.1795, was found for compound **10** (4-Cl) relative to 0.1557 (**1**). Oppositely, iodine in *ortho* position cause decrease of Δ_{charge} on O2 (C2=O) from 0.0453 (**1**) to 0.0225 (**11**; 2-I). If chlorine and iodine are in *meta* position they cause increase of electron density on N1 to 0.0025 and -0.0012 for compounds **9** (3-Cl) and **12** (3-I), relative to compound **1** (0.0048). Halogen in *para* position is also increasing the electron density on H1 (on N1) from 0, compound **1**, to -0.0034, compound **10** (4-Cl), and -0.0046, compound **13** (4-I). All halogen cause the decrease of electron density on imino nitrogen, N3 (C=N), and larger decrease from -0.1171 (**1**) to -0.0715 (**11**, 2-I) was noticed.

In the third group, the presence of strong electron-accepting nitro groups contributes to large differences in ICT process in comparison to the previous groups. Decrease of electron density at phenyl and increase on isatin heterocyclic ring were observed. The largest electron density decrease on C1', C3', C4', C5' and C6' was observed in compound **14** (2-NO₂) relative to comp. **1**: -0.0031 vs -0.0003 (C1'), -0.0456 vs -0.0163 (C3'), -0.0168 vs -0.0068 (C4'), -0.0583 vs -0.0304 (C5'), -0.0359 vs -0.0181 (C6') and -0.0335 vs -0.025 (C2'). Nitro group also causes electron density decrease on C2, C3, O2 (C2=O), N1 and N3 (C=N) atom, and the largest decrease was noticed in compound **14** (2-NO₂), while on C3 in compound **16** (4-NO₂) (Table S17). Imino nitrogen gained a amount of charge (Δ_{charge}), from -0.1171 (**1**) to -0.018 (**12**; 2-NO₂). Oppositely, the amount of charge (Δ_{charge}) in

compound **12** decreases on C2 relative to comp. **1**: 0.0494 vs 0.0272, O2 (C2=O): 0.0453 vs 0.0028, N1: 0.0048 vs -0.0076 and H1 (na N): 0 vs -0.005.

Z isomer:

The Δ_{charge} values for most of the *Z* isomers shows that electronic density was transferred from isatin heterocyclic ring to substituted phenyl ring. The difference appears in compound **7** where methoxy group in *para* position cause decrease electron density on phenyl and isatin ring. Compound **7** possesses the planar geometry which enable extended electron transfer from methoxy group to isatin ring (Table S10; $\theta = 0.01$). According to the type of ICT processes, presented in Fig. S28 and Tables S15–S17, the investigated compounds can be also separated into three groups: the first one includes compounds **2–7** with hydroxy and methoxy group, the second are compounds **8–13** along with halogen substituents, and the third ones are nitro substituted compounds **14–16**.

In the first group, in comp. **2** (2-OH) the electron density increase on C1' from -0.0013 (compound **1**) to -0.0167, C5' from -0.0081 to -0.0186 due to the positive resonance substituent effect. The presence of *hydroxy* group in *Z* isomer of compound **2** (2-OH) is decreasing the amount of electron density on carbonyl oxygen O2 (C2=O) from -0.0385 (compound **1**) to 0.0324, probably due to formation of intra-molecular hydrogen bonding [20]. The same effect cause decrease of Δ_{charge} on isatin carbonyl oxygen O2 (C2=O) from -0.0385 (compound **1**) to 0.0324 (compound **2**, 2-OH) and C2 carbon from 0.0442 (compound **1**) to 0.0533 (compound **2**, 2-OH). The presence of hydroxy and methoxy group in *para* position contribute to decrease of Δ_{charge} on C1' from -0.0013 (**1**) to -0.0098 (**4**, 4-OH) and -0.0037 (**7**, 4-OMe), respectively. In all hydroxy and methoxy isatin derivatives, except compound **7** (4-OMe), the increased electron density at C2' were noticed (Table S15).

In compound **7** the presence of *methoxy* group in *para* position cause the decrease of electron density on phenyl carbons, except C1', and isatin atoms: C2, C3, N1, and N3. Among the all *methoxy* substituted isatin derivatives, only in compound **7** (4-OMe) the amount of charge on *methoxy* carbon, oxygen and hydrogen atoms has a positive value comparing excited to ground state. The most pronounced decrease of electron density on C2' of compound **6**, from -0.0823 to -0.0177 (**1**), was obtained. The prominent change of Δ_{charge} on C3' was observed in compound **6** (3-OMe), from -0.0455 to -0.0022 (**1**), and

compound **7** (4-OMe), from 0 to -0.0455 (**1**), were obtained. The electron density on C5' during excitation decrease from -0.0081 (**1**) to -0.043 in compound **3** (3-OH) and to -0.0438 in compound **6** (3-OMe). Comprehensive comparison showed that the greatest change of Δ_{charge} on C2', C3', C4', C5' and C6' were found for compound **7** (4-OMe): 0.0013, 0, 0.0387, 0 and -0.0113 relative to compound **1** (Tables S15). Oppositely, in isatin heterocyclic ring the most pronounced change of electron density on C2 and C3 were observed in compound **7** (4-OMe): from 0.0442 (**1**) to -0.0445 on former, and from 0.1473 (**1**) to 0.0676 on latter carbon. The amount of charge on isatin nitrogen (N1) increase from -0.0048 to 0.0127 in compound **2** (2-OH), to -0.0012 in compound **4** (2-OH) and to 0.0029 in compound **5** (2-OMe) relative to compound **1**. On the other hand, the methoxy group in *para* position increase the electron density on isatin nitrogen (N1) to -0.0098. The amount of charge on imino nitrogen (N3 (C=N)) decrease from -0.0385 (compound **1**) to -0.0768 in compound **2** (2-OH), to -0.0622 in compound **7** (4-OMe).

In the second group, presence of chlorine atom cause change of Δ_{charge} on C1' for compound **8** (2-Cl) (-0.0004), comparing to -0.0013 (**1**). Both halogens cause increase of electron density on C2' and C5' relative to 0.0177 (**1**) for C2': -0.0693 (**9**, 3-Cl) and -0.066 (**12**, 3-I). Similar stand for C5' carbon: -0.0081 (**1**) vs -0.0437 (**9**; 3-Cl) and -0.0414 (**12**, 3-I) were noticed. The presence of halogen in *meta* and *para* positions also cause increase Δ_{charge} on C3' and C6': on C3' from -0.0455 (**1**) to -0.0014 (**9**, 3-Cl) and -0.0011 (**12**, 3-I) and on C6' from -0.0548 (**1**) to -0.0192 (**9**, 3-Cl) and -0.0181 (**12**, 3-I) respectively. On the other hand the iodine in *para* position increase electron density on C4': -0.0246 (**13**, 4-I) relative to -0.0155 (**1**) (Table S16). Iodine in *para* position also contribute to the decrease of electron density on carbonyl oxygen O2 (C2=O) from -0.0385 (**1**) to -0.015 (**13**; 4-I). Loses of Δ_{charge} on N1 was noted in compound **9** (3-Cl) from -0.007 to -0.0048 (**1**). Chlorine and iodine atom in *ortho* position causes decrease of electron density on imino nitrogen (N3) from -0.0385 (**1**) to -0.0232 (**8**, 2-Cl) and -0.0221 (**11**, 2-I).

The third group involves of *Z* isomers with nitro substituted compounds **14–16** which, in opposite to *E* isomers, showed less pronounced ICT processes. The presence of nitro group increases the electronic density at C5' carbon. The most prominent decrease in electron density on C5' from -0.0081 (**1**) to -0.0386 (**14**; 2-NO₂) was obtained. The nitro group in *ortho* position (compound **14**, 2-NO₂) cause an decrease of Δ_{charge} from -0.0177

(compound **1**) to -0.0418 comparing ground and excited state. The presence of nitro group causes the pronounced change of the electron density on C6' from -0.0548 (**1**) to -0.0267 (**14**; 4-NO₂). The electron accepting effect of nitro group cause decrease of the amount of Δ_{charge} on O2 (C2=O), N1 and N3 (C=N) atoms (Table S17). The greatest electron gain on carbonyl oxygen O2 was obtained for compound **14** (2-NO₂), i.e. -0.0526 relative to -0.0385 (**1**), -0.0099 on isatin nitrogen N1 of comp. **16** (4-NO₂) vs -0.0048 (**1**), and -0.0599 on imino nitrogen N3 (C=N) of comp. **14** (2-NO₂) vs -0.0385 (**1**).

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