Conformational communication between the Ar–CO and Ar–N axes in 2,2′-disubstituted benzanilides and their derivatives

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Benzanilides containing two or more potentially stereogenic amide axes exist in solution as mixtures of conformers which are detectable by NMR. For simple tertiary benzanilides carrying an *ortho* substituent on each ring, conformational control can be high (up to about 10 : 1) providing the substituents are large, indicating that the two axes are in conformational communication with one another. For more complex diamides, conformational communication breaks down, and mixtures of conformers are evident by NMR.

Introduction

Over the last few years there has been a growing interest in the preparation of non-biaryl atropisomers.[1,2] Because of the rigidity of the amide group, the most studied of these non-biaryl atropisomers have been either benzamide derivatives **1** or anilides **2** (Fig. 1). Our own work has concentrated primarily on *ortho*-substituted tertiary benzamides **1**,[3] in which the amide group lies more or less perpendicular to the plane of the aromatic ring.[3c] Provided rotation about the Ar–CO bond is slow enough, which is usually the case with 2,6-disubstituted benzamides (**1**: X, Y ≠ H), atropisomeric chirality results from this perpendicular arrangement. Even for less hindered compounds (mono-*ortho*-substituted benzamides for example, **1**: X or Y = H), transient chirality (on the NMR timescale) manifests itself spectroscopically in the diastereotopicity of groups attached to the ring or the amide nitrogen atom.

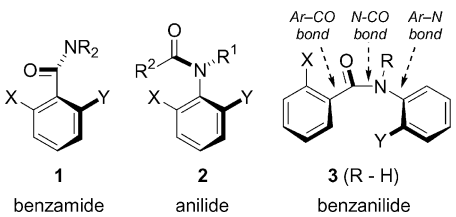


Fig. 1 Benzamides, anilides and benzanilides.

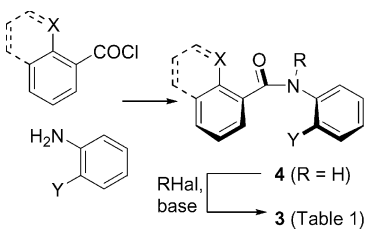
Axial chirality in *ortho*-substituted anilides **2** was recognized more than fifty years ago.[4,5] While differentially *N*,*N*-disubstituted amides generally prefer to exist as *Z*-rotamers (*i.e.* largest group *cis* to the oxygen) for steric reasons, it has been known for some time that *N*-alkyl acetanilides **2** (R^2 = Me)[6] and many *N*-alkyl benzanilides **2** (R^2 = Ar)[7] prefer to exist as the *E*-rotamer, which places the aryl group and the amide oxygen in the *trans* conformation, as shown for **2**. In general, atropisomerism is observed when an anilide carries two different non-hydrogen *ortho*-substituents X and Y. A large number of anilides with axial chirality have been described,[8] and we have recently reported that mono-*ortho*-substituted anilides may also exhibit chirality provided that the *ortho* substituent is iodo.[9]

We now report the preparation and conformational studies of compounds combining the amide structural motifs of both **1** and **2**—2,2′-disubstituted benzanilides **3** (Fig. 1). Using NMR, we demonstrate a degree of conformational interaction between the Ar–CO and N–CO axes, suggesting their potential application in stereochemical relay systems.[10]

Results and discussion

Conformational ratios in benzanilides

Compounds **3a–o** were prepared by the standard method shown in Scheme 1: available anilines and benzoyl chlorides were condensed to yield secondary anilides **4** (R = H). Alkylation of these compounds gave tertiary benzanilides **3a–o**, whose ^{1}H-NMR spectra at 25 °C in $CDCl_3$ show that they exist as a mixture of conformers about two or more of the Ar–CO, Ar–N and N–CO bonds in solution. All of these bonds are expected to rotate slowly on the NMR timescale at 25 °C, though fast on the laboratory timescale: typical barriers to rotation of such bonds in similar compounds lie in the region of 60–80 kJ mol^{-1}.[3h,9] Table 1 shows the ratios of the two or more conformers quantified by integration of the paired signals.



Scheme 1 Synthesis of 2,2′-disubstituted benzanilides.

The degree of conformational control is governed by the size of the substituents at the *ortho* positions (X and Y) and also the substituent at the nitrogen (R): the bulkier they are, the higher the conformational ratio. In **3a** (X = Y = I, R = Bn) and **3j** (X = NO_2, Y = I, R = Bn) the ratios reach a remarkable 10 : 1 and 12 : 1 respectively. Addition of a third bulky *ortho*-substituent, *i.e.* an

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Table 1 Conformational ratios of benzanilides **3a–o**

Compound	X	Y	R	Conformer ratio[a]
3a	I	I	Bn	10 : 1
3b	I	I	*o*-I–Bn	16 : 1.2 : 1
3c	I	I	Et	4.3 : 1
3d	I	I	i-Pr	2.5 : 1
3e	Benzo[b]	I	Bn	7 : 1
3f	Benzo[b]	CO_2Et	Bn	5 : 1
3g	Benzo[b]	CO_2H	Bn	3.25 : 1
3h	I	CO_2Et	Bn	5.3 : 1
3i	I	CO_2H	Bn	3.5 : 1
3j	NO_2	I	Bn	12 : 1
3k	NO_2	I	Et	6.4 : 1
3l	NO_2	I	Me	3.6 : 1
3m	NH_2	I	Bn	Broad
3n	NH_2	I	Et	Broad
3o	NH_2	I	Me	Broad

[a] Ratio in $CDCl_3$ at 25 °C. [b] 1-naphthamide.

extra iodo group at the *ortho* position of the *N*-benzyl group, adds a third conformer to the mixture: **3b** displays a conformational ratio of 16 : 1.2 : 1. The ratio between the two major conformers is nonetheless similar to the one observed for **3j**.

As the size of any of the substituents (X, Y or R) decreases, the conformational ratio also drops. For example, taking **3a** as a reference with X = Y = I and R = Bn, a reduction in size of any of the three groups shows lower ratios, as can be observed in **3c** and **3d** with a smaller R (Et, i-Pr), **3e** with a smaller X, and **3f** and **3g** with smaller Y groups.

The broad signals in the NMR spectra of **3m–o** indicate fast interconversion of the possible conformations, making determination of the conformational ratio impossible. In contrast, spectra of the analogous compounds with a NO_2 group, **3j–l**, have sharp signals characteristic of slow exchange. Fast Ar–CO rotation in **3m–o** is most likely due to stabilisation of the planar transition state for Ar–CO rotation by the electron-donating amino group.[3h]

Identification of the conformers

The X-ray crystal structures of **3a** and **3b** showed the expected *E*-rotamer[6,7] about the N–CO bond in the solid state, with the two iodo substituents on opposite faces of the plane of the amide, presumably in order to avoid steric interactions (Fig. 2 and 3). We confirmed that this *E-anti* conformer observed in the crystal structure is also the major conformer in solution by dissolving a crystal of **3a** in cold $CDCl_3$. The ^{1}H-NMR spectrum of this solution at low temperature showed a single conformer corresponding to the major conformer in the spectrum at room temperature. Allowing the solution to warm restored the 10 : 1 ratio. By contrast, a sample prepared at room temperature and cooled to −50 °C showed a mixture of conformers throughout.

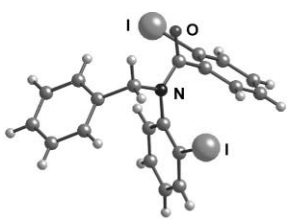


Fig. 2 X-Ray structure of **3a**.

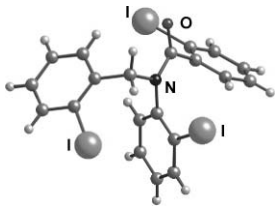
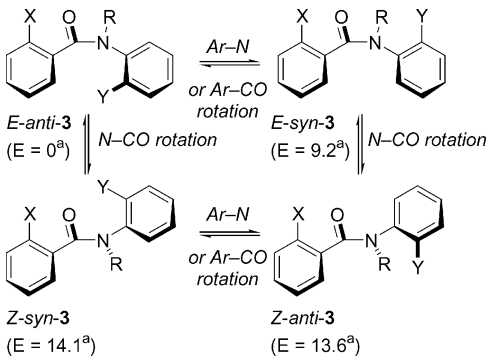


Fig. 3 X-Ray structure of **3b**.

Scheme 2 shows the four possible conformations of **3** that result from rotation about the Ar–N, Ar–CO and N–CO bonds, starting from the *E-anti* conformer. Molecular mechanics calculations (MMFF force field implemented by Spartan) for **3a** (X = Y = I; R = Bn) are in agreement with assignment of the *E-anti* conformation to the lowest energy conformer. The calculations also indicate that both *E* rotamers (*syn* and *anti*) have lower energy levels than the two *Z* rotamers. From this analysis we assume that the minor conformers observed by ^{1}H-NMR are the *E-syn* conformers, and that the ratios in Table 1 represent the ratio of *E-anti*-**3** to *E-syn*-**3**, with the exception of **3b**, in which another conformer is evident, probably a *Z* rotamer about the amide N–CO bond.



Scheme 2 Rotational interconversions in **3**. (a) Energy calculated (MMFF, Spartan) in kJ mol^{-1} relative to *E-anti*-**3** for X = Y = I; R = Bn.

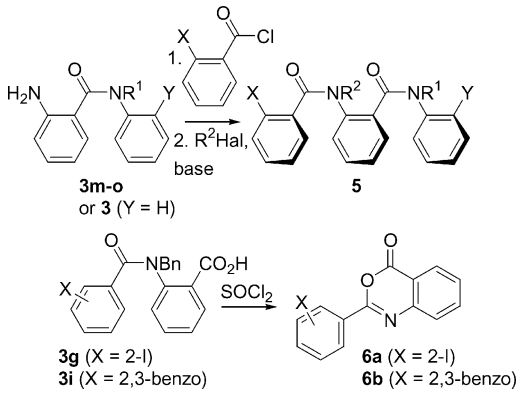
Variable temperature NMR studies of **3a**, **3b** and **3c** were carried out. **3a** and **3b** showed no change in their spectra over the range −50 to +50 °C in $CDCl_3$ or at +90 °C in d_6-DMSO, indicating that all three pertinent bond rotations have barriers of >75.1 kJ mol^{-1}. In contrast, VT NMR studies of **3c** in toluene (−70 to +100 °C) showed coalescence of the signals due to the two conformers of **3c**, allowing us to estimate a barrier to rotation for either the Ar–CO or Ar–N bond (whichever is the lower) of only 63.5 kJ mol^{-1}.

Conformational ratios in diamides

The high levels of conformational control in certain benzanilides **3** indicate that there is some degree of conformational communication between the Ar–CO and the N–CO axes, provided that the rings bear sufficiently large substituents. We recently reported a case in which conformational communication through a series of six Ar–CO axes facilitated the remote transmission of stereochemical information,[11] and with the aim of developing a similar system based on benzanilides we set about the synthesis of the diamides **5**. We were encouraged in this aim by reports that

N-alkylated oligo(*p*-benzamides)[12] and oligo(*m*-benzamides)[13] adopt a well-defined, helical secondary structure.

Our initial attempts to prepare diamides **5** from carboxylic acid derivatives of **3** (**3g** for example) *via* the acyl chloride led instead to the oxazinones **6** by cyclisation (Scheme 3). However, compounds **5a–o** were eventually successfully prepared by acylation of the amino derivatives **3m–o**, themselves produced by reduction of the nitro compounds **3j–l** (Scheme 3).



Scheme 3 Synthesis of the diamides **5**.

Table 2 shows the conformational ratios observed by ^{1}H-NMR at rt in $CDCl_3$ for compounds **5a–o**. Compounds **5a**, **5d**, **5f**, **5h**, **5k** and **5n**, with $R^2 = H$, are comparable conformationally to compounds **3** (Table 1) because a *secondary* amide cannot generate a stereogenic Ar–CO axis and will exist as the *Z* amide rotamer (Ar and C=O *cis*). These compounds display ratios from 22 : 1 to 5.5 : 1, depending on X, Y and R^1, suggesting that the benzoylamino groups allow good levels of stereocommunication between the two remaining axes in the molecule.[11]

Alkylation of the second amide group (*i.e.* introduction of $R^2 \neq H$) introduces a third (and if $X \neq H$, a fourth) potentially stereogenic axis to the molecule. Unfortunately, in all such cases, complex mixtures of conformers were observed: the two amide Ar–CO axes fail to interact with each other either directly or *via* the Ar–N axis. In the majority of the compounds the ratio between the conformers can be established by the integration of the signals corresponding to each conformer. However this becomes impossible in some cases—for example **5c** has a ^{1}H-NMR spectrum too complex for resolution of the signals of the individual conformers. In other cases, *e.g.* **5l** and **5m**, it is possible to identify the ratio of only the two major conformers (by integration of the signal corresponding to the methyl group). Other partly overlapping signals suggest that other conformers are populated, but in ratios that cannot be determined. In the absence of any *ortho* substituents, *i.e.* **5o**, faster interconversion between the conformers leads to broad signals.

Table 2 Conformational ratios of **5a–o**

Compound	X	Y	R^1	R^2	Ratio
5a	I	I	Bn	H	12 : 1
5b	I	I	Bn	CH_3	6.8 : 2 : 1
5c	I	I	Bn	Bn	Complex mixture
5d	NO_2	I	Bn	H	22 : 1
5e	NO_2	I	Bn	CH_3	4.5 : 1 : 1
5f	NO_2	I	CH_3	H	6.5 : 1
5g	NO_2	I	CH_3	Et	3.2 : 2.5 : 1.5 : 1
5h	NO_2	I	Et	H	5.5 : 1
5i	NO_2	I	Et	CH_3	4.5 : 2 : 1
5j	NO_2	I	CH_3	CH_3	4.2 : 4 : 1
5k	H	I	CH_3	H	4.5 : 1
5l	H	I	CH_3	Bn	1.33 : 1 : ?
5m	H	I	CH_3	Et	2 : 1 : ?
5n	H	H	Bn	H	8 : 1
5o	H	H	Bn	Bn	Broad

Molecular mechanic calculations (Spartan MMFF) suggest that in benzanilides with a bulky *ortho* substituent (here NR^2COAr) on the benzamide ring the *Z* rotamer becomes preferred to the *E* rotamer,[7] thus placing one amide group of **5** in the *E* conformation and the other in the *Z* (Fig. 4). Even with N–CO bonds orientated in this way, four or eight conformers can exist, and the differences in energy between them are minimal.

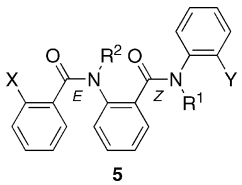


Fig. 4 Conformation of the diamide **5**.

Conformational communication between benzamide and anilide-type amide axes

With our conformational analysis of compounds **3** and **5** we have probed the ability of a pair of amide axes connected either as shown in Fig. 5A or Fig. 5B to communicate with one another: the results suggest that communication can be successful (subject to the size of the substituents) for A but is not successful for B. Compounds of type C, which contain two adjacent benzamide-type amide axes, are known in many cases to display high levels of conformational control,[3f,3t,14] and a detailed publication presenting out findings in this area is in preparation.[15] A final pairing—bis-anilides of type D—was investigated by Cheng *et al.*[16] but with tertiary amide groups **7d** exists as a mixture of conformers in solution.[17] In the solid state the typical[7] *E*-rotamer about the N–CO bond (Ar and C=O *trans*) is observed, with the two anilide groups disposed *anti*. In the crystal structure of **7e**, however, in which the *ortho* positions carry a fluorine atom, while the anilides are still *anti*, the unexpected opposite *Z* N–CO rotamer is populated,[7,18] an effect possibly related to the calculated switch from the *E* to the *Z* conformation in one of the amide bonds of **5**.

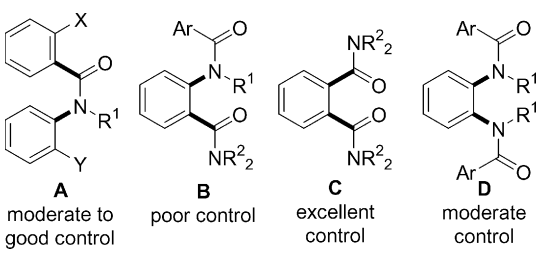
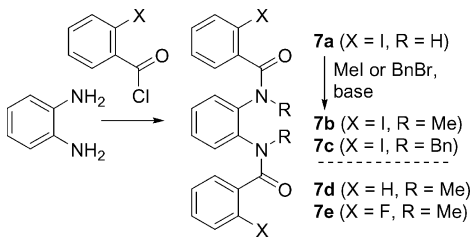


Fig. 5 Conformational communication between pairs of amide axes (axes are represented by bold bonds).

We prepared **7b** and **7c** (Scheme 4) with *ortho*-iodo substituents in order to slow the rotation about the bonds associated with the amide groups with the aim of establishing the conformational ratios in such compounds in solution. The ^{1}H-NMR spectrum showed a simple 5 : 1 ratio between only two conformers of **7b** at rt in $CDCl_3$. In the solid state, **7b** adopted a conformation with both N–CO bonds *Z* and the anilides *anti*, comparable to that reported for **7e**[18]—the X-ray crystal structure of **7b** is shown in Fig. 6. We assume that this is the major conformer in solution, but we have no evidence to allow assignment of the conformation of the minor conformer. It is notable that each crystal of **7b** contains only one enantiomeric conformer—the crystals have a chiral space group: monoclinic *P*2(1).[19] An analogue, **7c**, carrying *N* benzyl groups, showed only broad signals in its ^{1}H-NMR spectrum.



Scheme 4 Synthesis of the diamides **7**.

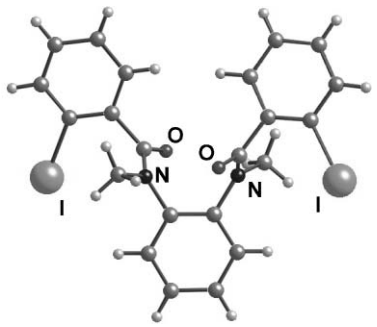


Fig. 6 X-Ray crystal structure of **7b**.

Conclusion

Conformational analysis of representative members of three classes of aromatic amides and diamides—compounds **3a–o** for those represented as Fig. 5A, **5a–n**, for those represented as Fig. 5B, and **7b** for those represented as Fig. 5D—shows that for compounds of types A and D moderate to high levels of conformational control can be achieved when the amides carry bulky substituents. Type B compounds **5** with two tertiary amide groups exist as complex conformational mixtures whereas the analogous compounds with *meta*[13] and *para*[12] substituted amides exist largely as single conformers. Poor control in this situation may be due to population of the usually disfavoured (for anilides) *Z* N–CO conformer, a feature also seen in **7**. Type C compounds, as previously reported,[3f,3h,3t] show excellent conformational control in solution, and a detailed report concerning this class of compounds is in preparation.[15]

Experimental

^{1}H and ^{13}C-NMR spectra were recorded on a Varian XL 300 MHz or Bruker Ultrashield 500 MHz instrument. VT NMR studies were recorded on an Inova 300 MHz instrument. NMR data are presented as follows: chemical shift δ (in ppm relative to $\delta_{TMS} = 0$), multiplicity, coupling constant *J* (quoted in hertz, Hz), integration, and assignment. IR spectra were recorded on an ATi Matson Genesis Series Fourier Transform spectrometer. Wavelengths of maximum absorbance are quoted in wavenumbers (cm^{-1}). Low resolution mass spectra (EI and CI) were recorded on a Fisons VG Trio 2000 quadrupole mass spectrometer. High resolution mass spectra were recorded on a Kratos Concept-IS mass spectrometer. Analytical TLC was carried out on Machery-Nagel pre-coated 0.2 mm silica plates with fluorescent indicator on aluminium. Flash column chromatography was carried out using Fluorochem Davisil 40–63 μm 60 A silica under a positive pressure of air. Conformational ratios were calculated by integration of the NMR signals corresponding to the same proton(s) relating to each conformer. When only two conformers are observed they are referred to as major and minor conformers, when more than two are observed they are referred to as conformers A, B, C··· listed in decreasing ratio. The purity of compounds **5b**, **5c**, **5e**, **5g**, **5l**, **5m**, **5o** and **7b** was confirmed by HPLC (Supelcosil LC 18 DB 4.6 mm × 250 mm, 90 : 10 hexane–isopropanol, flow 0.5 mL min^{-1}).

2-Iodo-*N*-(2-iodophenyl)benzamide 4a

To a solution of 2-iodoaniline (1 g, 4.56 mmol) and triethylamine (3.2 ml, 22.9 mmol) in ethyl acetate (25 mL) was added a solution of 2-iodobenzoyl chloride (1.22 g, 4.58 mmol) in ethyl acetate (25 mL). The mixture was stirred at rt under nitrogen overnight. The resulting suspension was filtered and the solid was washed with ether and $NaHCO_3$ aqueous saturated solution to yield the title compound as a white solid (1.1 g, 53%). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 6.91 (td, $J = 7.8$ and 1.5 Hz, 1H), 7.18 (td, $J = 7.8$ and 1.5 Hz, 1H), 7.41 (d, $J = 7.5$ Hz, 1H), 7.47 (t, $J = 7.5$ Hz, 1H), 7.58 (d, $J = 7.5$ Hz, 1H), 7.75 (bs, 1H), 7.83 (dd, $J = 8.1$ and 1.5 Hz, 1H), 7.97 (dd, $J = 8.1$ and 1 Hz, 1H), 7.97 (d, $J = 8.1$ Hz, 1H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 90.3 (Cq), 92.5 (Cq), 122.3 (CH), 126.6 (CH), 128.1 (CH), 128.4 (CH), 129.4 (CH), 131.7 (CH), 137.9 (Cq), 138.9 (CH), 140.4 (CH), 141.6 (Cq), 167.2 (Cq). IR (film) 3245, 1650 cm^{-1}. HRMS calcd for $C_{13}H_9ONI_2$: 448.8768. Found: 448.8776. Anal. calcd for $C_{13}H_9NOI_2$ (449.0)·1/4 H_2O: C, 34.43; H, 2.11; N, 3.09. Found: C, 34.18; H, 1.87; N, 2.99%. Mp 184–185 °C.

N-(2-Iodophenyl)-1-naphthamide 4b

To a solution of 2-iodoaniline (1 g, 4.56 mmol) and triethylamine (3.2 ml, 22.9 mmol) in ethyl acetate (50 mL) was slowly added 1-naphthoyl chloride (0.7 mL, 4.64 mmol). The mixture was stirred overnight at rt under nitrogen. The resulting suspension was filtered and the solid was washed with ether and $NaHCO_3$ aqueous saturated solution to yield the title compound as a yellow solid (909 mg, 53%). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 6.92 (ddd, $J = 7.8$, 7.5 and 1.5 Hz, 1H), 7.45 (td, $J = 8.4$ and 1.2 Hz, 1H), 7.53–7.64 (m, 3H), 7.84 (dd, $J = 7.8$ and 1.5 Hz, 1H), 7.87 (dd, $J = 8.4$ and 1.2 Hz, 1H), 7.92 (dd, $J = 7.5$ and 1.8 Hz, 1H), 8.01

(d, $J = 8.4$ Hz, 1H), 8.08 (bs, 1H), 8.48–8.54 (m, 2H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 90.7 (Cq), 122.1 (CH), 124.8 (CH), 125.3 (CH), 125.4 (CH), 126.3 (CH), 126.7 (CH), 127.5 (CH), 128.4 (CH), 129.4 (CH), 130.2 (Cq), 131.5 (CH), 133.8 (Cq), 133.9 (Cq), 138.5 (Cq), 138.9 (CH), 167.4 (Cq). IR (film) 3248 and 1648 cm^{-1}. HRMS calcd for $C_{17}H_{13}NOI$: 374.0036. Found: 374.0044. Anal. calcd for $C_{17}H_{12}NOI$ (373.2): C, 54.71; H, 3.24; N, 3.75. Found: C, 54.71; H, 3.14; N, 3.68%. Mp 160–161 °C.

Ethyl 2-(1-naphthamido)benzoate 4c

To a solution of 2-ethoxycarbonilaniline (1 g, 6.05 mmol) and triethylamine (4.5 mL, 32.3 mmol) in ethyl acetate (50 mL) was slowly added 1-naphthoyl chloride (0.91 mL, 6.04 mmol). The mixture was stirred overnight at rt under nitrogen. The mixture was diluted with ethyl acetate and washed with water. The aqueous layer was extracted with ethyl acetate and the combined organic layers were dried, filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (DCM) to yield **4c** (1.14 g, 58%). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.37 (t, $J = 7.2$ Hz, 3H), 4.33 (q, $J = 7.2$ Hz, 2H), 7.17 (ddd, $J = 8.1$, 7.2 and 1.2 Hz, 1H), 7.53–7.61 (m, 3H), 7.66 (td, $J = 7.2$ and 1.5 Hz, 1H), 7.88 (dd, $J = 7.2$ and 1.2 Hz, 1H), 7.90 (dd, $J = 7.8$ and 1.2 Hz, 1H), 7.98 (d, $J = 8.4$ Hz, 1H), 8.12 (dd, $J = 8.1$ and 1.8 Hz, 1H), 8.54 (dd, $J = 8.1$ and 1.5 Hz, 1H), 9.03 (dd, $J = 8.4$ and 0.9 Hz, 1H), 11.74 (bs, 1H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 14.1 (CH_3), 61.4 (CH_2), 115.6 (Cq), 120.5 (CH), 122.8 (CH), 124.9 (CH), 125.4 (CH), 125.6 (CH), 126.4 (CH), 127.2 (CH), 128.3 (CH), 130.4 (Cq), 130.9 (CH), 131.3 (CH), 133.9 (Cq), 134.5 (Cq), 134.6 (CH), 141.7 (Cq), 167.9 (Cq), 168.2 (Cq). IR (film) 3261, 1675 cm^{-1}. HRMS calcd for $C_{20}H_{18}NO_3$: 320.1281. Found: 320.1281. Anal. calcd for $C_{20}H_{17}NO_3$ (319): C, 75.22; H, 5.37; N, 4.39. Found: C, 74.79; H, 5.39; N, 4.35%. Mp 83–84 °C.

Ethyl 2-(2-iodobenzamido)benzoate 4d

To a solution of 2-iodobenzoylchloride (1.63 g, 6.12 mmol) and triethylamine (4.2 mL, 30.1 mmol) in ethyl acetate (50 mL) was added ethyl 2-aminobenzoate (0.9 mL, 6.09 mmol), and the mixture was stirred overnight at rt under nitrogen. The mixture was basified with $NaHCO_3$ aqueous saturated solution and extracted with DCM. The organic layer was dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (DCM) to yield **4d** (1.94 g, 80%). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.43 (t, $J = 7.2$ Hz, 3H), 4.39 (q, $J = 7.2$ Hz, 2H), 7.18 (td, $J = 7.5$ and 1.8 Hz, 1H), 7.19 (td, $J = 7.5$ and 1.2 Hz, 1H), 7.48 (td, $J = 7.5$ and 1.2 Hz, 1H), 7.60 (dd, $J = 7.8$ and 1.8 Hz, 1H), 7.67 (dd, $J = 7.5$ and 1.5 Hz, 1H), 7.98 (dd, $J = 8.1$ and 1.2 Hz, 1H), 8.13 (dd, $J = 8.1$ and 1.8 Hz, 1H), 8.93 (d, $J = 7.8$ Hz, 1H), 11.48 (bs, 1H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 14.1 (CH_3), 61.5 (CH_2), 92.7 (Cq), 115.7 (Cq), 120.5 (CH), 123.0 (CH), 128.0 (CH), 128.3 (CH), 130.9 (CH), 131.4 (CH), 134.6 (CH), 140.4 (CH), 141.2 (Cq), 142.0 (Cq), 167.6 (Cq), 168.1 (Cq). IR (film) 3257, 1680 cm^{-1}. HRMS calcd for $C_{16}H_{15}NO_3I$: 396.0091. Found: 396.0091. Anal. calcd for $C_{16}H_{14}NO_3I$ (395.2): C, 48.63; H, 3.57; N, 3.54. Found: C, 48.61; H, 3.64; N, 3.54%. Mp 53–54 °C.

N-(2-Iodophenyl)-2-nitrobenzamide 4e

To a solution of 2-iodoaniline (2.13 g, 9.72 mmol) and pyridine (2.6 mL, 32.2 mmol) in DCM (30 mL) was slowly added 2-nitrobenzoyl chloride (2 g, 9.70 mmol). The mixture was stirred overnight at rt under nitrogen. Petroleum ether was added and the resulting suspension was filtered and the solid was washed with $NaHCO_3$ aqueous saturated solution to yield the title compound (3.54 g, 99%). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 6.98 (td, $J = 7.5$ and 1.5 Hz, 1H), 7.47 (t, $J = 7.5$ Hz, 1H), 7.66–7.82 (m, 3H), 7.87 (dd, $J = 7.8$ and 1.5 Hz, 1H), 8.19 (d, $J = 8.1$ Hz, 1H), 8.33 (d, $J = 6.9$ Hz, 1H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 90.8 (Cq), 123.0 (CH), 124.9 (CH), 127.0 (CH), 128.3 (CH), 129.5 (CH), 131.1 (CH), 132.5 (Cq), 134.0 (CH), 137.6 (Cq), 138.9 (CH), 146.6 (Cq), 164.2 (Cq). IR (film) 1635 cm^{-1}. HRMS calcd for $C_{13}H_{10}O_3N_2I$: 368.9731. Found: 368.9727. Mp 182 °C.

N-Benzyl-2-nitro-*N*-phenylbenzamide 4f

To a solution of 2-nitrobenzoyl chloride (90%, 658 mg, 3.20 mmol) in DCM (12 mL), were added pyridine (1 mL, 12.38 mmol) and aniline (0.3 mL, 3.29 mmol), and the mixture was stirred overnight at rt under nitrogen. The mixture was basified with $NaHCO_3$ aqueous saturated solution and extracted with DCM. The organic layer was washed with HCl 2 M, dried and filtered and the solvent was removed under reduced pressure. The residue was dissolved in dry THF (40 mL), and NaH (60%, 406 mg, 10.15 mmol) and benzyl bromide (1.6 mL, 13.4 mmol) were added and the mixture was stirred overnight at rt under nitrogen. The solvent was removed under reduced pressure, the residue was partitioned between ethyl acetate and water, and the aqueous phase was extracted with ethyl acetate. The organic extracts were dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 50%) to yield **4f** (1.06 g, quantitative). ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 4.96 (s, 2H), 6.73–6.76 (m, 2H), 6.86–6.89 (m, 3H), 7.06–7.17 (m, 7H), 7.23–7.27 (m, 1H), 7.73 (d, $J = 8$ Hz, 1H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 52.9 (CH_2), 124.3 (CH), 127.6 (CH), 127.8 (CH), 128.2 (CH), 128.5 (CH), 128.9 (CH), 129.1 (CH), 129.29 (CH), 129.34 (CH), 133.26 (Cq), 133.34 (CH), 136.6 (Cq), 141.1 (Cq), 155.7 (Cq), 167.1 (Cq). IR (film) 1651 cm^{-1}. HRMS calcd for $C_{20}H_{16}N_2O_3Na$: 355.1053. Found: 355.1051. Mp 97–99 °C.

2-Amino-*N*-benzyl-*N*-phenylbenzamide 4g

To a solution of **4f** (1 g, 3.00 mmol) in DMF (30 mL) was added $SnCl_2 \cdot H_2O$ (7.7 g, 34.1 mmol). The mixture was stirred at rt for 24 h and was basified with $NaHCO_3$ aqueous saturated solution and extracted with DCM. The organic extracts were washed with brine, dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ethereum ether to AcOEt) to yield **4g** (783 mg, 86%). ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 4.52 (bs, 2H), 5.02 (s, 2H), 6.21 (td, $J = 7.5$ and 1 Hz, 1H), 6.53 (dd, $J = 8.1$ and 1 Hz, 1H), 6.66 (dd, $J = 7.8$ and 1.5 Hz, 1H), 6.83–6.87 (m, 3H), 6.93–6.97 (m, 1H), 6.98–7.03 (m, 2H), 7.10–7.22 (m, 6H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 53.3 (CH_2), 116.6 (CH), 116.9 (CH), 119.9 (Cq), 126.5 (CH), 126.9 (2CH), 127.3 (CH), 128.1 (2CH), 128.5 (2CH), 128.9 (2CH), 129.6 (CH), 130.5 (CH), 137.5 (Cq), 143.6 (Cq), 146.4 (Cq), 170.9 (Cq). IR (film)

3359 and 1619 cm^{-1}. HRMS calcd for $C_{20}H_{19}N_2O$: 303.1492. Found: 303.1501.

2-Iodo-*N*-benzyl-*N*-(2-iodophenyl)benzamide 3a

To a suspension of NaH (60%, 37 mg, 0.92 mmol) in THF (5 mL) were added 2-iodo-*N*-(2-iodophenyl)benzamide **4a** (110 mg, 0.24 mmol) and benzyl bromide (110 μL, 0.92 mmol). The mixture was stirred overnight at rt under nitrogen. The mixture was diluted with ethyl acetate and washed with water. The organic layer was dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 20%) to yield **3a** (110 mg, 91%). ^{1}H-NMR ($CDCl_3$, 300 MHz) major conformer δ 4.22 (d, J = 14.1 Hz, 1H), 6.00 (d, J = 14.1 Hz, 1H), 6.83–6.76 (m, 1H), 6.86 (dd, J = 5.7 and 1.8 Hz, 1H), 6.91 (dd, J = 6.9 and 1.5 Hz, 1H), 6.93 (dd, J = 6.9 and 1.5 Hz, 1H), 7.08 (ddd, J = 7.8, 7.5 and 1.2 Hz, 1H), 7.26–7.29 (m, 3H), 7.37–7.40 (m, 3H), 7.66 (dd, J = 8.1 and 1.2 Hz, 1H), 7.79 (dd, J = 7.8 and 1.2 Hz, 1H). Minor conformer δ 4.60 (d, J = 14.1 Hz, 1H), 4.73 (d, J = 14.1 Hz, 1H), 6.76–8.01 (m, 13H masked by the major conformer). Ratio 10 : 1. ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 51.3 (CH_2), 94.0 (Cq), 99.3 (Cq), 126.4 (CH), 127.3 (CH), 127.7 (CH), 128.1 (CH), 128.6 (CH), 129.5 (CH), 130.0 (CH), 131.8 (CH), 136.0 (Cq), 139.2 (CH), 139.8 (CH), 141.4 (Cq), 142.8 (Cq), 169.5 (Cq). IR (film) 1655 cm^{-1}. HRMS calcd for $C_{20}H_{16}NOI_2$: 539.9316. Found: 539.9321. Mp 118–119 °C.

2-Iodo-*N*-(2-iodobenzyl)-*N*-(2-iodophenyl)benzamide 3b

To a suspension of NaH (60%, 40 mg, 1 mmol) in THF (5 mL) were added 2-iodo-*N*-(2-iodophenyl)benzamide **4a** (104 mg, 0.23 mmol) and 2-iodobenzyl bromide (276 mg, 0.93 mmol). The mixture was stirred overnight at rt under nitrogen. The mixture was diluted with ethyl acetate and washed with water. The organic layer was dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 25%) to yield **3b** (140 mg, 88%). ^{1}H-NMR ($CDCl_3$, 300 MHz) conformer A δ 4.62 (d, J = 14.5 Hz, 1H), 6.00 (d, J = 14.5 Hz, 1H), 6.80 (dd, J = 7.5 and 1.5 Hz, 1H), 6.82 (dd, J = 7.5 and 1.5 Hz, 1H), 6.85 (dd, J = 7.5 and 1.5 Hz, 1H), 6.92 (dd, J = 7.5 and 1.5 Hz, 1H), 6.95 (dd, J = 7.5 and 1.5 Hz, 1H), 7.09 (ddd, J = 7.8, 7.5 and 1.2 Hz, 1H), 7.37 (ddd, J = 7.8, 7.5 and 1.5 Hz, 1H), 7.42 (dd, J = 7.8 and 1.5 Hz, 1H), 7.66 (dd, J = 7.8 and 1.5 Hz, 1H), 7.67 (dd, J = 7.8 and 1.5 Hz, 1H), 7.77 (dd, J = 7.8 and 1.5 Hz, 1H), 8.07 (dd, J = 7.8 and 1.5 Hz, 1H). Conformer B δ 4.81 (d, J = 14.5 Hz, 1H), 5.97 (d, J = 14.5 Hz, 1H), 6.78–8.09 (m, 12H masked by the major conformer). Conformer C δ 4.89 (d, J = 14.5 Hz, 1H), 4.99 (d, J = 14.5 Hz, 1H), 6.78–8.09 (m, 12H masked by the major conformer). ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 54.4 (CH_2), 93.9 (Cq), 100.5 (Cq), 100.8 (Cq), 126.7 (CH), 127.4 (CH), 128.5 (CH), 128.8 (CH), 129.5 (CH), 129.7 (CH), 130.1 (CH), 131.6 (CH), 131.7 (CH), 139.1 (CH), 139.26 (CH), 139.27 (Cq), 140.0 (CH), 141.0 (Cq), 142.2 (Cq), 170.0 (Cq). Ratio 16 : 1.2 : 1. IR (film) 1650 cm^{-1}. HRMS calcd for $C_{20}H_{14}NOI_3Na$: 687.8102. Found: 687.8089. Mp 182–184 °C.

2-Iodo-*N*-ethyl-*N*-(2-iodophenyl)benzamide 3c

To a suspension of NaH (60%, 70 mg, 1.75 mmol) in THF (5 mL) was added 2-iodo-*N*-(2-iodophenyl)benzamide **4a** (199 mg, 0.40 mmol) and iodoethane (100 μL, 1.24 mmol). The mixture was stirred at rt under nitrogen overnight. The mixture was diluted with ethyl acetate and washed with water. The organic layer was dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether–AcOEt 10%) to yield **3c** (196 mg, 92%). ^{1}H-NMR ($CDCl_3$, 300 MHz) major conformer δ 1.29 (dd, J = 7.2 and 6.9 Hz, 3H), 3.22 (dq, J = 14 and 6.9 Hz, 1H), 4.63 (dq, J = 14 and 7.2 Hz, 1H), 6.81 (dd, J = 7.5 and 1.5 Hz, 1H), 6.89 (dd, J = 7.5 and 1.5 Hz, 1H), 7.07 (td, J = 7.5 and 1.2 Hz, 1H), 7.16 (td, J = 7.5 and 1.5 Hz, 1H), 7.29 (dd, J = 7.5 and 1.5 Hz, 1H), 7.41 (dd, J = 7.8 and 1.5 Hz, 1H), 7.69 (dd, J = 7.8 and 1.2 Hz, 1H), 7.81 (dd, J = 7.8 and 1.5 Hz, 1H). Minor conformer δ 1.10 (dd, J = 6.9 and 7.2 Hz, 3H), 3.53 (m, 2H), 6.80–7.50 (m, 6H masked by the major conformer), 7.89 (dd, J = 7.8 and 1.2 Hz, 1H), 7.96 (d, J = 7.8 Hz, 1H). Ratio 4.3 : 1. ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 12.2 (CH_3), 43.3 (CH_2), 94.1 (Cq), 99.7 (Cq), 126.2 (CH), 127.4 (CH), 128.6 (CH), 129.4 (CH), 129.9 (CH), 130.9 (CH), 139.0 (CH), 139.9 (CH), 141.6 (Cq), 143.1 (Cq), 169.2 (Cq). IR (film) 1651 cm^{-1}. HRMS calcd for $C_{15}H_{14}NOI_2$: 477.9159. Found: 477.9163. Mp 139–140 °C.

2-Iodo-*N*-(2-iodophenyl)-*N*-isopropylbenzamide 3d

To a solution of 2-iodo-*N*-isopropylaniline[20] (174 mg, 0.67 mmol) and pyridine (0.27 mL, 3.68 mmol) in dry DCM (6 mL) was added 2-iodobenzoyl chloride (268 mg, 1.00 mmol). The mixture was stirred overnight at rt under nitrogen. The mixture was diluted with DCM and washed with saturated aqueous $NaHCO_3$. The organic layer was dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 10%) to yield **3d** (246 mg, 75%). ^{1}H-NMR ($CDCl_3$, 300 MHz) major conformer δ 1.29 (d, J = 6.6 Hz, 3H), 1.66 (d, J = 6.6 Hz, 3H), 4.61 (h, J = 6.6 Hz, 1H), 6.81 (dd, J = 7.5 and 1.5 Hz, 1H), 6.90 (dd, J = 7.5 and 1.5 Hz, 1H), 7.11 (td, J = 7.5 and 1.2 Hz, 1H), 7.21 (td, J = 7.5 and 1.5 Hz, 1H), 7.60 (dd, J = 7.8 and 1.5 Hz, 1H), 7.62 (dd, J = 7.8 and 1.5 Hz, 1H), 7.65 (dd, J = 7.8 and 1.5 Hz, 1H), 7.79 (dd, J = 7.8 and 1.5 Hz, 1H). Minor conformer δ 1.16 (d, J = 6.7 Hz, 3H), 1.34 (d, J = 6.7 Hz, 3H), 4.13 (h, J = 6.7 Hz, 1H), 6.81–7.72 (m, 6H masked by the major conformer), 7.91 (d, J = 7.8 Hz, 1H), 8.00 (d, J = 7.8 Hz, 1H). Ratio 2.5 : 1. ^{13}C-NMR ($CDCl_3$, 75.5 MHz) major conformer δ 19.4 (CH_3), 21.6 (CH_3), 51.5 (CH), 93.9 (Cq), 102.8 (Cq), 126.6 (CH), 127.1 (CH), 128.6 (CH), 129.4 (CH), 129.7 (CH), 130.9 (CH), 139.0 (CH), 140.0 (CH), 142.1 (Cq), 142.8 (Cq), 169.7 (Cq). Minor conformer δ 20.8 (CH_3), 23.7 (CH_3), 52.8 (CH), 92.9 (Cq), 102.3 (Cq), 126.7 (CH), 128.0 (CH), 128.9 (CH), 129.4 (CH), 130.1 (CH), 130.8 (CH), 139.4 (CH), 140.1 (CH), 169.4 (Cq). IR (film) 1649 cm^{-1}. HRMS calcd for $C_{16}H_{16}NOI_2$: 491.9316. Found: 491.9322. Mp 161–162 °C.

***N*-Benzyl-*N*-(2-iodophenyl)-1-naphthamide 3e**

To a suspension of NaH (60%, 94 mg, 2.35 mmol) in THF (10 mL) was added *N*-(2-iodophenyl)-1-naphthamide **4b** (257 mg, 0.69 mmol) and benzyl bromide (350 μL, 2.93 mmol). The mixture was stirred overnight at rt under nitrogen. The mixture was diluted with ethyl acetate and washed with water. The organic layer was dried and filtered and the solvent was removed under reduced

pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 20%) to yield **3e** (296 mg, 93%). ^{1}H-NMR ($CDCl_3$, 300 MHz) major conformer δ 4.32 (d, J = 14.1 Hz, 1H), 6.12 (d, J = 14.1 Hz, 1H), 6.37 (m, 1H), 6.66 (m, 1H), 7.16 (d, J = 7.2 Hz, 1H), 7.19 (d, J = 7.2 Hz, 1H), 7.27–7.53 (m, 7H), 7.63 (d, J = 8.4 Hz, 1H), 7.70–7.73 (m, 1H), 7.74 (d, J = 7.2, 1H), 8.09 (d, J = 8.4 Hz, 1H). Minor conformer δ 4.54 (bd, J = 14.1 Hz, 1H), 4.82 (m, 1H), 4.40–7.99 (m, 16H masked by the major conformer). Ratio 7 : 1. ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 51.6 (CH_2), 99.4 (Cq), 123.7 (CH), 124.2 (CH), 125.2 (CH), 125.9 (CH), 126.6 (CH), 127.7 (CH), 128.1 (2CH), 128.4 (2CH), 129.0 (CH), 129.1 (CH), 129.6 (2CH), 130.2 (Cq), 131.3 (CH), 133.1 (Cq), 133.6 (Cq), 136.8 (Cq), 139.8 (CH), 143.4 (Cq), 170.0 (Cq). IR (film) 1649 cm^{-1}. HRMS calcd for $C_{24}H_{19}NOI$: 464.0506. Found: 464.0507. Anal. calcd for $C_{24}H_{18}NOI$ (463.3)·1/4 H_2O: C, 61.62; H, 3.99; N, 2.99. Found: C, 61.55; H, 3.98; N, 2.94%. Mp 182–184 °C.

Ethyl 2-(*N*-benzyl-1-naphthamido)benzoate 3f

To a suspension of NaH (60%, 111 mg, 2.77 mmol) in THF (10 mL) were added ethyl 2-(1-naphthamido)benzoate **4c** (251 mg, 0.79 mmol) and benzyl bromide (400 μL, 3.34 mmol). The mixture was stirred overnight at rt under nitrogen. The mixture was diluted with ethyl acetate and washed with water. The organic layer was dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 30%) to yield **3f** (193 mg, 60%). ^{1}H-NMR ($CDCl_3$, 300 MHz) major conformer δ 1.45 (t, J = 6.9 Hz, 3H), 4.28 (d, J = 14.4 Hz, 1H), 4.36–4.49 (m, 2H), 6.21 (d, J = 14.4 Hz, 1H), 6.59 (d, J = 7.8 Hz, 1H), 6.94 (td, J = 7.5 and 1.5 Hz, 1H), 7.06 (td, J = 7.5 and 1.2 Hz, 1H), 7.15 (d, J = 8.1 Hz, 1H), 7.17 (d, J = 8.1 Hz, 1H), 7.30–7.48 (m, 5H), 7.53 (dd, J = 8.4 and 1.5 Hz, 1H), 7.55 (dd, J = 8.4 and 1.5 Hz, 1H), 7.64 (d, J = 8.1 Hz, 1H), 7.73 (d, J = 8.4 Hz, 1H), 7.76 (dd, J = 7.5 and 1.5 Hz, 1H), 8.17 (d, J = 8.1 Hz, 1H). Minor conformer δ 1.48 (t, J = 6.9 Hz, 3H), 4.35–4.49 (m, 4H masked by the major conformer), 6.88–7.98 (m, 15H masked by the major conformer), 8.11 (dd, J = 7.5 and 1.5 Hz, 1H). Ratio 5 : 1. ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 14.1 (CH_3), 53.1 (CH_2), 61.4 (CH_2), 124.1 (CH), 124.6 (CH), 125.3 (CH), 125.8 (CH), 126.4 (CH), 127.46 (CH), 127.50 (CH), 128.0 (CH), 128.2 (Cq), 128.4 (2CH), 128.9 (CH), 129.3 (2CH), 130.2 (Cq), 130.9 (CH), 131.3 (CH), 131.9 (CH), 133.1 (Cq), 133.8 (Cq), 137.4 (Cq), 141.7 (Cq), 164.5 (Cq), 169.5 (Cq). IR (film) 1718 and 1648 cm^{-1}. HRMS calcd for $C_{27}H_{24}NO_3$: 410.1751. Found: 410.1750. Anal. calcd for $C_{27}H_{23}NO_3$ (409.5)·1/4 H_2O: C, 78.34; H, 5.72; N, 3.38. Found: C, 78.20; H, 5.81; N, 3.28%.

2-(*N*-Benzyl-1-naphthamido)benzoic acid 3g

To a solution of **3f** (516 mg, 0.99 mmol) in EtOH (10 mL) was added NaOH 40% aqueous solution (40 mL) and the mixture was stirred at reflux temperature for 3 h. The mixture was acidified with HCl 6 N and extracted with ethyl acetate. The organic extracts were dried and filtered and the solvent was removed under reduced pressure to yield **3g** (468 mg, 97%). ^{1}H-NMR ($CDCl_3$, 300 MHz) major conformer δ 4.33 (d, J = 14.4 Hz, 1H), 6.19 (d, J = 14.4 Hz, 1H), 6.61 (bd, J = 6.9 Hz, 1H), 6.98–7.04 (m, 1H), 7.10–7.21 (m, 3H), 7.30–7.59 (m, 7H), 7.67 (d, J = 8.1 Hz, 1H), 7.75 (d, J = 7.8 Hz, 1H), 7.91 (d, J = 7.5 Hz, 1H), 8.19 (d, J = 7.8 Hz, 1H). Minor conformer δ 4.60–5.00 (m, 4H), 6.87–6.89 (m, 1H), 6.99–7.76 (m, 13H masked by the major conformer), 7.98 (d, J = 7.5 Hz, 1H), 8.23 (d, J = 7.2 Hz, 1H). Ratio 3.25 : 1. ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 53.4 (CH_2), 124.4 (CH), 125.3 (CH), 126.0 (CH), 126.7 (CH), 126.9 (CH), 127.6 (CH), 127.8 (CH), 128.2 (CH), 128.3 (Cq), 128.5 (2CH), 129.2 (CH), 129.5 (2CH), 130.2 (Cq), 131.2 (CH), 132.3 (CH), 133.0 (CH), 133.2 (Cq), 133.7 (Cq), 137.2 (Cq), 142.4 (Cq), 169.7 (Cq), 170.1 (Cq). IR (film) 3060, 1718 and 1594 cm^{-1}. HRMS calcd for $C_{25}H_{19}NO_3Na$: 404.1257. Found: 404.1260.

Ethyl 2-(*N*-benzyl-2-iodobenzamido)benzoate 3h

To a solution of **4d** (1 g, 2.53 mmol), in dry THF (40 mL), were added NaH (60%, 320 mg, 8 mmol) and benzyl bromide (1.25 mL, 10.4 mmol) and the mixture was stirred overnight at rt under nitrogen. The mixture was diluted with ethyl acetate and washed with water. The organic layer was dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 40%) to yield **3h** (834 mg, 68%). ^{1}H-NMR ($CDCl_3$, 300 MHz) major conformer δ 1.53 (t, J = 7.1 Hz, 3H), 4.09 (d, J = 14.3 Hz, 1H), 4.52 (q, J = 7.1 Hz, 2H), 6.03 (d, J = 14.3 Hz, 1H), 6.83 (ddd, J = 8, 7.5 and 1.8 Hz, 1H), 6.96 (dd, J = 7.5 and 1.8 Hz, 1H), 7.06 (td, J = 7.5 and 1 Hz, 1H), 7.13–7.22 (m, 3H), 7.28–7.32 (m, 3H), 7.39–7.42 (m, 2H), 7.68 (dd, J = 8 and 1 Hz, 1H), 7.87 (dd, J = 7.5 and 1.8 Hz, 1H). Minor conformer δ 1.41 (t, J = 7.1 Hz, 3H), 4.30–4.80 (m, 4H masked by the major conformer), 6.80–7.44 (m, 8H masked by the major conformer), 7.50 (dd, J = 7.8 and 1.8 Hz, 1H), 7.55 (dd, J = 7.5 and 1 Hz, 1H), 7.78 (dd, J = 7.6 and 1 Hz, 1H), 7.94 (dd, J = 8 and 1 Hz, 1H), 8.02 (dd, J = 7.8 and 1.5 Hz, 1H). Ratio 5.3 : 1. ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 14.3 (CH_3), 52.9 (CH_2), 61.7 (CH_2), 94.0 (Cq), 127.1 (CH), 127.3 (CH), 127.5 (CH), 128.0 (CH), 128.2 (2CH), 129.6 (2CH), 129.7 (CH), 131.5 (2CH), 132.4 (CH), 136.5 (Cq), 139.1 (CH), 140.9 (Cq), 142.0 (Cq), 165.7 (Cq), 169.1 (Cq). IR (film) 1716 and 1652 cm^{-1}. HRMS calcd for $C_{23}H_{21}NO_3I$: 486.0561. Found: 486.0570. Anal. calcd for $C_{23}H_{20}NO_3I$ (485.3): C, 56.92; H, 4.15; N, 2.89. Found: C, 57.36; H, 4.28; N, 2.79%. Mp 102–104 °C.

2-(*N*-Benzyl-2-iodobenzamido)benzoic acid 3i

To a solution of **3h** (405 mg, 0.83 mmol) in EtOH (10 mL) was added NaOH 40% aqueous solution (30 mL) and the mixture was stirred at reflux temperature for 3 h. The mixture was acidified with HCl 6 N and extracted with DCM. The organic extracts were dried and filtered and the solvent was removed under reduced pressure to yield **3i** (382 mg, quantitative). ^{1}H-NMR ($CDCl_3$, 300 MHz) major conformer δ 4.90 (d, J = 14.4 Hz, 1H), 6.10 (d, J = 14.4 Hz, 1H), 6.84 (ddd, J = 7.8, 7.5 and 1.5 Hz, 1H), 7.00–7.12 (m, 2H), 7.17–7.35 (m, 6H), 7.42–7.45 (m, 2H), 7.70 (d, J = 7.8 Hz, 1H), 8.01 (dd, J = 7.5 and 1.8 Hz, 1H), 10.37 (br s, 1H). Minor conformer δ 4.67–4.73 (m, 1H), 4.86–4.91 (m, 1H), 7.00–7.75 (m, 11H masked by the major conformer), 7.97 (d, J = 7.8 Hz, 1H), 8.19 (dd, J = 7.8 and 1.2 Hz, 1H). Ratio 3.5 : 1. ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 53.2 (CH_2), 93.9 (Cq), 127.1 (Cq), 127.3 (CH), 127.5 (CH), 127.6 (CH), 128.26 (2CH), 128.30 (CH), 129.7 (2CH), 129.9 (CH), 131.6 (CH), 132.4 (CH), 133.3 (CH), 136.3 (Cq), 139.1 (CH), 141.4 (Cq), 141.6 (Cq), 169.6 (Cq), 169.7 (Cq).

IR (film) 3031, 1720 and 1596 cm^{-1}. HRMS calcd for $C_{21}H_{15}NO_3I$: 456.0102. Found: 456.0096.

N-Benzyl-*N*-(2-iodophenyl)-2-nitrobenzamide 3j

To a solution of **4e** (1.2 g, 3.26 mmol), in dry THF (40 mL), were added NaH (60%, 460 mg, 11.5 mmol) and benzyl bromide (1.6 mL, 13.4 mmol) and the mixture was stirred overnight at rt under nitrogen. The solvent was evaporated under reduced pressure. The residue was partitioned between ethyl acetate and water, and the aqueous phase was extracted with ethyl acetate. The organic extracts were dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 50%) to yield **3j** (1.43 g, 96%). ^{1}H-NMR ($CDCl_3$, 300 MHz) major conformer δ 4.31 (d, $J = 14.1$ Hz, 1H), 6.01 (d, $J = 14.1$ Hz, 1H), 6.72 (dd, $J = 7.8$ and 1.8 Hz, 1H), 6.83 (td, $J = 7.5$ and 1.8 Hz, 1H), 6.93 (td, $J = 7.5$ and 1.5 Hz, 1H), 7.30–7.42 (m, 6H), 7.51 (td, $J = 7.5$ and 1.5 Hz, 1H), 7.75 (dd, $J = 7.8$ and 1.5 Hz, 1H), 7.80 (dd, $J = 7.8$ and 1.5 Hz, 1H), 7.97 (dd, $J = 8.1$ and 1.5 Hz, 1H). Minor conformer δ 4.71 (s, 2H), 6.70–7.81 (m, 10H masked by the major conformer), 7.90 (dd, $J = 7.8$ and 1.5 Hz, 1H), 7.91 (dd, $J = 7.8$ and 1.5 Hz, 1H), 8.35 (dd, $J = 8.1$ and 1.5 Hz, 1H). Ratio 12 : 1. ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 51.4 (CH_2), 99.5 (Cq), 124.2 (CH), 127.8 (CH), 127.9 (CH), 128.4 (2CH), 128.9 (CH), 129.7 (CH), 129.89 (CH), 129.92 (2CH), 131.2 (CH), 132.7 (Cq), 133.6 (CH), 135.5 (Cq), 140.0 (CH), 142.3 (Cq), 145.4 (Cq), 166.5 (Cq). IR (film) 1653, 1527 and 1346 cm^{-1}. HRMS calcd for $C_{20}H_{15}N_2O_3INa$: 481.0020. Found: 481.0016. Mp 158–160 °C.

N-Ethyl-*N*-(2-iodophenyl)-2-nitrobenzamide 3k

To a solution of **4e** (503 mg, 1.37 mmol), in dry THF (10 mL), were added NaH (60%, 257 mg, 6.4 mmol) and ethyl iodide (1 mL, 12.4 mmol) and the mixture was stirred overnight at rt under nitrogen. The solvent was evaporated under reduced pressure. The residue was partitioned between ethyl acetate and water, and the aqueous phase was extracted with ethyl acetate. The organic extracts were dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 50%) to yield **3k** (458 mg, 85%). ^{1}H-NMR ($CDCl_3$, 300 MHz) major conformer δ 1.34 (t, $J = 7.2$ Hz, 3H), 3.28 (dq, $J = 14$ and 7.2 Hz, 1H), 4.60 (dq, $J = 14$ and 7.2 Hz, 1H), 6.91 (td, $J = 7.5$ and 1.5 Hz, 1H), 7.16 (td, $J = 7.5$ and 1.5 Hz, 1H), 7.30 (dd, $J = 8.1$ and 1.5 Hz, 1H), 7.37 (ddd, $J = 8.1$, 7.5 and 1.5 Hz, 1H), 7.47 (td, $J = 7.5$ and 1.5 Hz, 1H), 7.61 (dd, $J = 7.5$ and 1.5 Hz, 1H), 7.82 (dd, $J = 7.8$ and 1.5 Hz, 1H), 7.98 (dd, $J = 7.5$ and 1.5 Hz, 1H). Minor conformer δ 1.06 (t, $J = 7.2$ Hz, 3H), 3.55 (q, $J = 7.2$ Hz, 2H), 6.8–8.0 (m, 7H masked by the major conformer), 8.29 (dd, $J = 8.1$ and 1.5 Hz, 1H). Ratio 6.4 : 1. ^{13}C-NMR ($CDCl_3$, 75.5 MHz) major conformer δ 11.6 (CH_3), 43.6 (CH_2), 100.1 (Cq), 124.2 (CH), 127.4 (CH), 129.2 (CH), 129.6 (CH), 129.8 (CH), 130.2 (CH), 132.9 (Cq), 133.6 (CH), 140.1 (CH), 143.2 (Cq), 166.1 (Cq). Minor conformer representative signals only, δ 13.3 (CH_3), 46.4 (CH_2), 124.8 (CH), 128.1 (CH), 129.7 (CH), 130.1 (CH), 134.5 (CH), 139.7 (CH), 145.9 (Cq). IR (film) 1655 cm^{-1}. HRMS calcd for $C_{15}H_{14}N_2O_3I$: 397.0044. Found: 397.0043.

N-Methyl-*N*-(2-iodophenyl)-2-nitrobenzamide 3l

To a solution of **4e** (501 mg, 1.36 mmol), in dry THF (10 mL), were added NaH (60%, 235 mg, 5.9 mmol) and methyl iodide (0.9 mL, 14.5 mmol) and the mixture was stirred overnight at rt under nitrogen. The solvent was evaporated under reduced pressure. The residue was partitioned between ethyl acetate and water, and the aqueous phase was extracted with ethyl acetate. The organic extracts were dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to AcOEt) to yield **3l** (407 mg, 78%). ^{1}H-NMR ($CDCl_3$, 300 MHz) major conformer δ 3.43 (s, 3H), 6.87 (td, $J = 7.5$ and 1.5 Hz, 1H), 7.14 (td, $J = 7.5$ and 1.5 Hz, 1H), 7.32 (dd, $J = 7.5$ and 1.5 Hz, 1H), 7.34 (ddd, $J = 8.1$, 7.5 and 1.5 Hz, 1H), 7.46 (td, $J = 7.5$ and 1.2 Hz, 1H), 7.62 (dd, $J = 7.5$ and 1.5 Hz, 1H), 7.76 (dd, $J = 7.5$ and 1.5 Hz, 1H), 7.95 (dd, $J = 8.1$ and 1.2 Hz, 1H). Minor conformer δ 3.09 (s, 3H), 7.10 (ddd, $J = 8.1$, 7.5 and 1.5 Hz, 1H), 7.50 (td, $J = 7.5$ and 1.5 Hz, 1H), 7.59–7.84 (m, 4H masked by the major conformer), 7.94 (dd, $J = 8.1$ and 1.2 Hz, 1H), 8.27 (dd, $J = 8.1$ and 1.2 Hz, 1H). Ratio 3.6 : 1. ^{13}C-NMR ($CDCl_3$, 75.5 MHz) major conformer δ 36.7 (CH_3), 99.1 (Cq), 124.2 (CH), 127.9 (CH), 128.9 (CH), 129.71 (CH), 129.75 (CH), 129.96 (CH), 132.7 (Cq), 133.6 (CH), 140.1 (CH), 145.1 (Cq), 167.1 (Cq). Minor conformer representative signals only, δ 39.1 (CH_3), 124.7 (CH), 128.2 (CH), 128.7 (CH), 129.8 (CH), 130.00 (CH), 130.1 (CH), 132.7 (CH), 134.8 (CH), 145.6 (Cq). IR (film) 1654 cm^{-1}. HRMS calcd for $C_{14}H_{12}N_2O_3I$: 382.9887. Found: 382.9883.

2-Amino-*N*-benzyl-*N*-(2-iodophenyl)benzamide 3m

To a solution of **3j** (400 mg, 0.87 mmol) in DMF (9 mL) was added $SnCl_2 \cdot H_2O$ (2.02g, 8.94 mmol). The mixture was stirred at rt for 24 h and it was basified with $NaHCO_3$ aqueous saturated solution and extracted with DCM. The organic extracts were washed with brine, dried and filtered and the solvent was removed under reduced pressure to yield the title compound **3m** (374 mg, quantitative). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 3.96 (bs, 2H), 4.39 (d, $J = 14.4$ Hz, 1H), 5.77 (d, $J = 14.4$ Hz, 1H), 6.34 (bs, 1H), 6.62 (d, $J = 7.8$ Hz, 1H), 6.71 (d, $J = 8.1$ Hz, 1H), 6.82–7.03 (m, 4H), 7.20–7.37 (m, 5H), 7.82 (d, $J = 7.8$ Hz, 1H). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 51.8 (CH_2), 99.2 (Cq), 116.0 (CH), 116.2 (CH), 118.8 (Cq), 127.3 (CH), 128.1 (CH), 128.2 (2CH), 128.5 (2CH), 128.6 (CH), 129.0 (CH), 130.5 (CH), 131.1 (CH), 136.4 (Cq), 139.7 (CH), 144.4 (Cq), 146.7 (Cq), 170.5 (Cq). IR (film) 3364 and 1634 cm^{-1}. HRMS calcd for $C_{20}H_{18}N_2OI$: 429.0458. Found: 429.0462.

2-Amino-*N*-ethyl-*N*-(2-iodophenyl)benzamide 3n

To a solution of **3k** (458 mg, 1.16 mmol) in DMF (10 mL) was added $SnCl_2 \cdot H_2O$ (2.77 g, 12.3 mmol). The mixture was stirred at rt for 24 h and it was basified with $NaHCO_3$ aqueous saturated solution and extracted with DCM. The organic extracts were washed with brine, dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to AcOEt) to yield **3n** (417 mg, 98%). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.21 (t, $J = 7.2$ Hz, 3H), 3.44–3.55 (m, 1H), 4.29 (bs, 1H), 4.65 (bs, 2H), 6.31 (bs, 1H), 6.58 (d, $J = 7.5$ Hz, 1H), 6.80–7.20 (m, 5H), 7.84 (d, $J = 7.2$ Hz, 1H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 12.2 (CH_3), 44.5 (CH_2), 99.9

(Cq), 116.7 (CH), 116.8 (CH), 119.9 (Cq), 128.6 (CH), 129.0 (CH), 129.2 (CH), 130.9 (CH), 131.1 (CH), 140.3 (CH), 147.0 (Cq), 170.9 (Cq). IR (film) 3360 and 1620 cm^{-1}. HRMS calcd for $C_{15}H_{16}N_2OI$: 367.0302. Found: 367.0302.

2-Amino-*N*-(2-iodophenyl)-*N*-methylbenzamide 3o

To a solution of **3l** (595 mg, 1.56 mmol) in DMF (10 mL) was added $SnCl_2 \cdot H_2O$ (3.7 g, 16.40 mmol). The mixture was stirred at rt for 24 h and it was basified with $NaHCO_3$ aqueous saturated solution and extracted with DCM. The organic extracts were washed with brine, dried and filtered and the solvent was removed under reduced pressure to yield **3o** (548 mg, quantitative). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 3.36 (s, 3H), 4.73 (bs, 2H), 6.39 (bs, 1H), 6.69 (d, J = 8.4 Hz, 1H), 6.83–7.21 (m, 5H), 7.83 (d, J = 7.8 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 37.8, (CH_3), 98.8 (Cq), 116.8 (CH), 119.1 (Cq), 129.1 (CH), 129.7 (CH), 131.1 (CH), 140.3 (CH), 147.2 (Cq), 171.4 (Cq). IR (film) 3358 and 1620 cm^{-1}.

***N*-Benzyl-*N*-(2-iodophenyl)-2-(2-iodobenzamido)benzamide 5a**

To a solution of **3m** (389 mg, 0.91 mmol) and pyridine (0.5 mL, 6.18 mmol) in DCM (5 mL) was added 2-iodobenzoyl chloride (97%, 250 mg, 0.91 mmol). The mixture was stirred at rt for 24 h and it was basified with $NaHCO_3$ aqueous saturated solution and extracted with DCM. The organic extracts were dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (DCM to DCM–MeOH 0.5%) to yield **5a** (436 mg, 73%). ^{1}H-NMR ($CDCl_3$, 300 MHz) major conformer δ 4.35 (d, J = 14.4 Hz, 1H), 5.72 (d, J = 14.4 Hz, 1H), 6.75–6.72 (m, 2H), 6.91 (ddd, J = 7.8, 7.5 and 1.5 Hz, 1H), 7.03 (dd, J = 7.8 and 1.5 Hz, 1H), 7.13 (ddd, J = 7.8, 7.5 and 1.5 Hz, 1H), 7.19–7.40 (m, 6H), 7.49–7.51 (m, 2H), 7.82 (dd, J = 8.1 and 1.5 Hz, 1H), 7.99 (d, J = 7.8 Hz, 1H), 8.38 (d, J = 8.1 Hz, 1H), 9.73 (s, 1H). Minor conformer δ 4.57–4.64 (m, 1H), 5.21–5.27 (m, 1H), other signals masked by the major conformer. Ratio 12 : 1. ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 53.7 (CH_2), 92.8 (Cq), 99.8 (Cq), 122.5 (CH), 122.8 (CH), 124.4 (Cq), 127.76 (CH), 127.79 (CH), 128.2 (CH), 128.3 (CH), 128.4 (2CH), 128.9 (CH), 129.3 (2CH), 130.8 (CH), 131.3 (CH), 131.4 (CH), 136.1 (Cq), 137.1 (Cq), 140.1 (CH), 140.3 (CH), 141.7 (Cq), 144.1 (Cq), 167.1 (Cq), 169.5 (Cq). IR (film) 3338, 1683 and 1632 cm^{-1}. HRMS calcd for $C_{27}H_{20}N_2O_2I_2Na$: 680.9506. Found: 680.9507. Mp 112–114 °C.

***N*-Benzyl-*N*-(2-iodophenyl)-2-(2-iodo-*N*-methylbenzamido)benzamide 5b**

To a solution of **5a** (95 mg, 0.14 mmol), in dry THF (5 mL), were added NaH (60%, 30 mg, 0.75 mmol) and methyl iodide (0.1 mL, 1.60 mmol) and the mixture was stirred overnight at rt under nitrogen. The residue was partitioned between DCM and water, and the aqueous phase was extracted with DCM. The organic extracts were dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 30%) to yield **5b** (90 mg, 93%). ^{1}H-NMR ($CDCl_3$, 300 MHz) conformer A δ 3.24 (br s, 3H), 4.55 (d, J = 14.5 Hz, 1H), 6.72 (d, J = 14.5 Hz, 1H), 6.81–7.94 (m, 17H). Conformer B δ 4.90 (d, J = 15 Hz, 1H), 5.20 (d, J = 15 Hz, 1H), other signals masked by the major conformer. Conformer C δ 4.32 (d, J = 14 Hz, 1H), 6.98 (d, J = 14 Hz, 1H), other signals masked by the major conformer. Ratio 6.8 : 2 : 1. ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 41.5 (CH_3), 53.1 (CH_2), 92.0 (Cq), 98.2 (Cq), 126.9 (CH), 127.3 (2CH), 128.32 (2CH), 128.41 (CH), 128.44 (CH), 128.5 (CH), 129.0 (CH), 129.1 (CH), 129.5 (CH), 130.1 (CH), 130.9 (CH), 133.6 (Cq), 133.9 (CH), 136.8 (Cq), 138.8 (CH), 139.8 (CH), 141.8 (Cq), 142.3 (Cq), 144.5 (Cq), 167.4 (Cq), 170.7 (Cq). IR (film) 1652 cm^{-1}. HRMS calcd for $C_{28}H_{22}N_2O_2I_2Na$: 694.9663. Found: 694.9672. Mp 156–158 °C. HPLC 5.49 min.

***N*-Benzyl-*N*-(2-iodophenyl)-2-(*N*-benzyl-2-iodobenzamido)benzamide 5c**

To a solution of **5a** (200 mg, 0.30 mmol), in dry THF (5 mL), was added NaH (60%, 54 mg, 1.35 mmol) and benzyl bromide (0.2 mL, 1.67 mmol) and the mixture was stirred overnight at rt under nitrogen. The mixture was partitioned between ethyl acetate and water, and the aqueous phase was extracted with ethyl acetate. The organic extracts were dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 30%) to yield **5c** (227 mg, quantitative). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 3.78–6.22 (m, 4H), 6.65–8.09 (m, 22H). IR (film) 1649 cm^{-1}. HRMS calcd for $C_{34}H_{26}N_2O_2I_2Na$: 770.9976. Found: 770.9987. HPLC 5.48 min.

***N*-Benzyl-*N*-(2-iodophenyl)-2-(2-nitrobenzamido)benzamide 5d**

To a solution of **3m** (1 g, 2.34 mmol) and pyridine (1 mL, 12.4 mmol) in DCM (15 mL) was added 2-nitrobenzoyl chloride (90%, 486 mg, 2.35 mmol). The mixture was stirred at rt for 24 h and it was basified with $NaHCO_3$ aqueous saturated solution and extracted with DCM. The organic extracts were dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (DCM) to yield **5d** (1.14 g, 85%). ^{1}H-NMR ($CDCl_3$, 500 MHz) major conformer δ 4.34 (d, J = 14.3 Hz, 1H), 4.65 (d, J = 14.3 Hz, 1H), 6.75–6.79 (m, 2H), 6.89 (ddd, J = 8, 7.5 and 1.5 Hz, 1H), 7.00 (dd, J = 7.5 and 1.5 Hz, 1H), 7.11 (ddd, J = 8, 7.5 and 1.5 Hz, 1H), 7.15–7.30 (m, 5H), 7.58 (dd, J = 7.5 and 1 Hz, 1H), 7.66 (td, J = 8 and 1.5 Hz, 1H), 7.75 (td, J = 7.5 and 1 Hz, 1H), 7.81 (dd, J = 8 and 1.5 Hz, 1H), 8.13 (d, J = 8.5 Hz, 1H), 8.27 (d, J = 8.5 Hz, 1H), 9.79 (s, 1H). Minor conformer δ 4.61 (d, J = 15 Hz, 1H), 5.25 (d, J = 15 Hz, 1H), other signals masked by the major conformer. Ratio 22 : 1. ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 52.9 (CH_2), 99.2 (Cq), 122.6 (CH), 123.1 (CH), 124.4 (Cq), 124.7 (CH), 127.7 (CH), 128.0 (CH), 128.24 (CH), 128.28 (2CH), 129.18 (CH), 129.28 (2CH), 129.34 (CH), 130.7 (CH), 130.9 (CH), 131.5 (CH), 133.0 (Cq), 133.8 (CH), 135.9 (Cq), 136.8 (Cq), 140.2 (CH), 144.2 (Cq), 146.6 (Cq), 164.1 (Cq), 169.6 (Cq). IR (film) 3329, 1688 and 1633 cm^{-1}. HRMS calcd for $C_{27}H_{20}N_3O_4INa$: 600.0391. Found: 600.0393.

***N*-Benzyl-*N*-(2-iodophenyl)-2-(*N*-methyl-2-nitrobenzamido)benzamide 5e**

To a solution of **5d** (103 mg, 0.18 mmol), in dry THF (5 mL), were added NaH (60%, 35 mg, 0.87 mmol) and methyl iodide (0.1 mL, 1.60 mmol) and the mixture was stirred overnight at rt under nitrogen. The residue was partitioned between DCM and water, and the aqueous phase was extracted with DCM. The

organic extracts were dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 50%) to yield **5e** (105 mg, quantitative). ^{1}H-NMR ($CDCl_3$, 300 MHz) conformer A δ 3.23 (br s, 3H), 4.53 (d, $J = 14.5$ Hz, 1H), 5.72 (d, $J = 14.5$ Hz, 1H), 6.86–7.66 (m, 13H), 6.90 (dd, $J = 7.7$ and 1.5 Hz, 1H), 7.50 (dd, $J = 7.9$ and 1 Hz, 1H), 7.94 (dd, $J = 7.9$ and 1.4 Hz, 1H), 8.25 (dd, $J = 7.6$ and 1.8 Hz, 1H). Conformer B δ 4.88 (d, $J = 15$ Hz, 1H), 5.14 (d, $J = 15$ Hz, 1H), other signals masked by the major conformer. Conformer C δ 4.32 (d, $J = 13.8$ Hz, 1H), 5.98 (d, $J = 13.8$ Hz, 1H), other signals masked by the major conformer. Ratio 4.5 : 1 : 1. ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 41.2 (CH_3), 53.2 (CH_2), 98.3 (Cq), 124.5 (CH), 127.0 (CH), 127.3 (CH), 128.2 (3CH), 128.3 (CH), 129.1 (CH), 129.2 (2CH), 129.4 (CH), 129.6 (CH), 131.1 (CH), 133.0 (Cq), 133.5 (Cq), 133.6 (CH), 134.6 (CH), 137.1 (Cq), 139.8 (CH), 141.3 (Cq), 144.5 (Cq), 144.8 (Cq), 167.8 (Cq), 168.3 (Cq). IR (film) 1652 and 1529 cm^{-1}. HRMS calcd for $C_{28}H_{23}N_3O_4I$: 592.0728. Found: 592.0734. HPLC 5.59 min.

N-(2-Iodophenyl)-*N*-methyl-2-(2-nitrobenzamido)benzamide 5f

To a solution of **3o** (371 mg, 1.05 mmol) and pyridine (0.5 mL, 6.19 mmol) in DCM (5 mL) was added 2-nitrobenzoyl chloride (0.9%, 222 mg, 1.07 mmol). The mixture was stirred overnight at rt and it was basified with $NaHCO_3$ aqueous saturated solution and extracted with DCM. The organic extracts were dried, filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 50%) to yield **5f** (460 mg, 87%). ^{1}H-NMR ($CDCl_3$, 300 MHz) major conformer δ 3.36 (s, 3H), 6.77 (t, $J = 7.5$ Hz, 1H), 6.91 (d, $J = 8$ Hz, 1H), 6.97 (dd, $J = 8$ and 1.5 Hz, 1H), 7.20–7.29 (m, 3H), 7.63–7.76 (m, 3H), 7.81 (d, $J = 8$ Hz, 1H), 8.10 (d, $J = 8$ Hz, 1H), 8.27 (d, $J = 8.3$ Hz, 1H), 9.97 (br s, 1H). Minor conformer δ 7.14–7.07 (m, 2H), 7.46–7.52 (m, 2H), 7.81–7.96 (m, 1H), 8.39–8.43 (m, 1H), 9.45 (s, 1H), other signals masked by the major conformer. Ratio 6.5 : 1. ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 37.8 (CH_3), 98.4 (Cq), 122.8 (CH), 123.2 (CH), 124.0 (CH), 124.8 (Cq), 128.6 (CH), 128.7 (CH), 129.2 (CH), 129.8 (CH), 129.9 (CH), 130.8 (CH), 131.0 (CH), 133.0 (Cq), 133.9 (CH), 137.0 (Cq), 140.1 (CH), 146.5 (Cq), 146.7 (Cq), 164.2 (Cq), 170.1 (Cq). IR (film) 3306, 1686, 1631 and 1529 cm^{-1}. HRMS calcd for $C_{21}H_{17}N_3O_4I$: 502.0258. Found: 502.0264.

N-(2-Iodophenyl)-*N*-methyl-2-(*N*-ethyl-2-nitrobenzamido)benzamide 5g

To a solution of **5f** (98 mg, 0.2 mmol), in dry THF (5 mL), were added NaH (60%, 39 mg, 0.97 mmol) and ethyl iodide (0.2 mL, 2.48 mmol) and the mixture was stirred at rt under nitrogen overnight. The residue was partitioned between ethyl acetate and water, and the aqueous phase was extracted with ethyl acetate. The organic extracts were dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 50%) to yield **5g** (93 mg, 90%). ^{1}H-NMR ($CDCl_3$, 300 MHz) conformer A δ 0.86–1.51 (m, 3H), 3.17–3.85 (m, 1H), 3.27 (s, 3H), 4.78–4.93 (m, 1H), 6.80–8.12 (m, 11H), 8.28–8.32 (m, 1H). Conformer B δ 3.42 (s, 3H), other signals masked by major conformer. Conformer C δ 3.23 (s, 3H), other signals masked by major conformer. Conformer D δ 3.46 (s, 3H), other signals masked by major conformer. Ratio 3.2 : 2.5 : 1.5 : 1. IR (film) 1649 and 1528 cm^{-1}. HRMS calcd for $C_{23}H_{21}N_3O_4I$: 530.0571. Found: 530.0560. HPLC 4.49 min.

N-Ethyl-*N*-(2-iodophenyl)-2-(2-nitrobenzamido)benzamide 5h

To a solution of **3n** (417 mg, 1.14 mmol) and pyridine (0.5 mL, 6.19 mmol) in DCM (5 mL) was added 2-nitrobenzoyl chloride (0.9%, 260 mg, 1.26 mmol). The mixture was stirred at rt overnight and it was basified with $NaHCO_3$ aqueous saturated solution and extracted with DCM. The organic extracts were dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 50%) to yield **5h** (524 mg, 89%). ^{1}H-NMR ($CDCl_3$, 300 MHz) major conformer δ 1.18 (t, $J = 7.2$ Hz, 3H), 3.53 (dq, $J = 7.2$ and 6.9 Hz, 1H), 4.25 (dq, $J = 7.2$ and 6.9 Hz, 1H), 6.77 (ddd, $J = 7.8$, 7.5 and 1.2 Hz, 1H), 6.92 (dd, $J = 7.5$ and 1.2 Hz, 1H), 6.97 (dd, $J = 7.5$ and 1.2 Hz, 1H), 7.14 (dd, $J = 7.8$ and 1.5 Hz, 1H), 7.21–7.31 (m, 2H), 7.61–7.79 (m, 3H), 7.84 (dd, $J = 7.8$ and 1.2 Hz, 1H), 8.13 (d, $J = 8.1$ Hz, 1H), 8.26 (d, $J = 8.1$ Hz, 1H), 9.91 (br s, 1H). Minor conformer δ 1.15–1.21 (m, 1H, masked by the major conformer), 3.63–3.77 (m, 1H), 3.81–3.95 (m, 1H), 6.77–8.30 (m, 12H, masked by the major conformer), 9.22 (br s, 1H). Ratio 5.5 : 1. ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 12.1 (CH_3), 44.8 (CH_2), 99.4 (Cq), 122.8 (CH), 123.2 (CH), 124.6 (Cq), 124.8 (CH), 128.3 (CH), 128.7 (CH), 129.2 (CH), 129.5 (CH), 130.8 (CH), 130.9 (CH), 131.2 (CH), 133.1 (Cq), 134.1 (CH), 136.9 (Cq), 140.3 (CH), 144.4 (Cq), 146.4 (Cq), 165.0 (Cq), 170.6 (Cq). IR (film) 3307, 1682 and 1632 cm^{-1}. HRMS calcd for $C_{22}H_{19}N_3O_4I$: 516.0415. Found: 516.0406.

N-Ethyl-*N*-(2-iodophenyl)-2-(*N*-methyl-2-nitrobenzamido)benzamide 5i

To a solution of **5h** (99 mg, 0.19 mmol), in dry THF (5 mL), were added NaH (60%, 43 mg, 1.07 mmol) and methyl iodide (0.15 mL, 2.40 mmol) and the mixture was stirred overnight at rt under nitrogen. The residue was partitioned between ethyl acetate and water, and the aqueous phase was extracted with ethyl acetate. The organic extracts were dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 50%) to yield **5i** (102 mg, quantitative). ^{1}H-NMR ($CDCl_3$, 300 MHz) conformer A δ 1.16 (t, $J = 6.9$ Hz, 3H), 3.28 (s, 3H), 3.66 (dq, $J = 7.2$ and 6.9 Hz, 1H), 4.58 (dq, $J = 7.2$ and 6.9 Hz, 1H), 6.76–7.68 (m, 8H), 7.79–8.01 (m, 3H), 8.22–8.27 (m, 1H). Conformer B δ 1.12 (t, $J = 7.2$ Hz, 3H), 3.20 (s, 3H), 3.53–3.60 (m, 1H), 3.95 (dq, $J = 7.5$ and 7.2 Hz, 1H), 6.76–8.27 (m, 12H, masked by the major conformer). Conformer C δ 3.52 (s, 3H), other signals masked by major conformer. Ratio 4.5 : 2 : 1. IR (film) 1650 and 1529 cm^{-1}. HRMS calcd for $C_{23}H_{21}N_3O_4I$: 530.0571. Found: 530.0577.

N-(2-Iodophenyl)-*N*-methyl-2-(*N*-methyl-2-nitrobenzamido)benzamide 5j

To a solution of **5f** (94 mg, 0.19 mmol), in dry THF (5 mL), were added NaH (60%, 38 mg, 0.95 mmol) and methyl iodide (0.15 mL, 2.41 mmol) and the mixture was stirred overnight at rt under nitrogen. The residue was partitioned between ethyl

acetate and water, and the aqueous phase was extracted with ethyl acetate. The organic extracts were dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 50%) to yield **5j** (54 mg, 56%). ^{1}H-NMR ($CDCl_3$, 300 MHz) conformer A δ 3.28 (s, 3H), 3.43 (s, 3H), 6.83–8.27 (m, 12H). Conformer B δ 3.22 (s, 3H), 3.31 (s, 3H), 6.83–8.27 (m, 12H). Conformer C δ 3.46 (s, 3H), 3.58 (s, 3H), 6.83–8.27 (m, 12H). Ratio 4.2 : 4 : 1. IR (film) 1657, 1650 and 1529 cm^{-1}. HRMS calcd for $C_{22}H_{19}N_3O_4I$: 516.0415. Found: 516.0411.

2-Benzamido-*N*-(2-iodophenyl)-*N*-methylbenzamide 5k

To a solution of **3o** (399 mg, 1.13 mmol) and pyridine (0.5 mL, 6.19 mmol) in DCM (5 mL) was added benzoyl chloride (0.2 mL, 1.72 mmol). The mixture was stirred at rt overnight and it was basified with $NaHCO_3$ aqueous saturated solution and extracted with DCM. The organic extracts were dried, filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 50%) to yield **5k** (335 mg, 65%). ^{1}H-NMR ($CDCl_3$, 500 MHz) major conformer δ 3.41 (s, 3H), 6.71 (t, J = 7.5 Hz, 1H), 6.91 (t, J = 7.5 Hz, 1H), 6.97 (d, J = 7.5 Hz, 1H), 7.10 (d, J = 7.3 Hz, 1H), 7.23–7.29 (m, 2H), 7.52–7.57 (m, 3H), 7.78 (d, J = 7.7 Hz, 1H), 8.04 (d, J = 7 Hz, 2H), 8.48 (d, J = 8.3 Hz, 1H), 10.70 (s, 1H). Minor conformer δ 3.34 (s, 3H), 7.65–7.70 (m, 1H), 7.94–8.00 (m, 2H), 8.50–8.57 (m, 1H), 10.05 (s, 1H), other signals masked by the major conformer. Ratio 4.5 : 1. ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 38.0 (CH_3), 98.5 (Cq), 121.9 (CH), 122.1 (CH), 122.9 (Cq), 127.3 (2CH), 128.8 (2CH), 129.0 (CH), 129.1 (CH), 129.57 (CH), 129.60 (CH), 131.1 (CH), 131.9 (CH), 134.6 (Cq), 138.3 (Cq), 140.3 (CH), 146.7 (Cq), 165.0 (Cq), 170.6 (Cq). IR (film) 3337, 1676 and 1634 cm^{-1}. HRMS calcd for $C_{21}H_{18}N_2O_2I$: 457.0407. Found: 457.0406.

2-(*N*-Benzylbenzamido)-*N*-(2-iodophenyl)-*N*-methylbenzamide 5l

To a solution of **5k** (93 mg, 0.20 mmol), in dry THF (5 mL), were added NaH (60%, 30 mg, 0.75 mmol) and benzyl bromide (0.1 mL, 0.84 mmol) and the mixture was stirred overnight at rt under nitrogen. The mixture was partitioned between ethyl acetate and water, and the aqueous phase was extracted with ethyl acetate. The organic extracts were dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 50%) to yield **5l** (81 mg, 73%). ^{1}H-NMR ($CDCl_3$, 300 MHz) conformer A δ 3.25 (s, 3H), 4.24 (d, J = 15 Hz, 1H), 6.05 (d, J = 15 Hz, 1H), 6.55–7.97 (m, 18H). Conformer B δ 3.42 (s, 3H) other signals masked by major conformer. Other conformers masked. Ratio 1.33 : 1 : ?. IR (film) 1651 cm^{-1}. HRMS calcd for $C_{28}H_{23}N_2O_2INa$: 569.0696. Found: 569.0697. HPLC 5.45 min.

2-(*N*-Ethylbenzamido)-*N*-(2-iodophenyl)-*N*-methylbenzamide 5m

To a solution of **5k** (90 mg, 0.197 mmol), in dry THF (5 mL), were added NaH (60%, 45 mg, 1.125 mmol) and ethyl iodide (0.2 mL, 2.49 mmol) and it was stirred at rt under nitrogen overnight. The mixture was partitioned between ethyl acetate and water, and the aqueous phase was extracted with ethyl acetate. The organic extracts were dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 50%) to yield **5m** (67 mg, 70%). ^{1}H-NMR ($CDCl_3$, 300 MHz) conformer A δ 1.25 (t, J = 6.9 Hz, 3H), 3.23 (s, 3H), 3.60–3.90 (m, 2H), 6.54–7.98 (m, 12H). Conformer B δ 3.36 (s, 3H), 4.34–4.51 (m, 1H), 4.60–4.74 (m, 1H) other signals masked by the major conformer. Other conformers masked. Ratio 2 : 1 : ?. IR (film) 1647 cm^{-1}. HRMS calcd for $C_{23}H_{21}N_2O_2INa$: 507.0540. Found: 507.0542. HPLC 5.48 min.

2-Benzamido-*N*-benzyl-*N*-phenylbenzamide 5n

To a solution of **4g** (780 mg, 2.58 mmol) and pyridine (1 mL, 12.4 mmol) in DCM (10 mL) was added benzoyl chloride (0.4 mL, 3.44 mmol). The mixture was stirred overnight at rt and it was basified with $NaHCO_3$ aqueous saturated solution and extracted with DCM. The organic extracts were dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 50%) to yield **5n** (1.03 g, 98%). ^{1}H-NMR ($CDCl_3$, 500 MHz) major conformer δ 5.16 (s, 2H), 6.71 (ddd, J = 8, 7.5 and 1 Hz, 1H), 6.87–6.90 (m, 2H), 6.93 (dd, J = 7.5 and 1 Hz, 1H), 7.09–7.17 (m, 3H), 7.21–7.23 (m, 3H), 7.25–7.30 (m, 3H), 7.52 (dd, J = 7.5 and 7 Hz, 2H), 7.58 (ddd, J = 7.5, 7 and 1.5 Hz, 1H), 7.98 (d, J = 8.5 Hz, 1H), 8.40 (dd, J = 8.5 and 1 Hz, 1H), 10.51 (s, 1H). Minor conformer δ 7.46 (dd, J = 8 and 7.5 Hz, 1H), 8.10 (dd, J = 8.5 and 1 Hz, 1H), other signals masked by the major conformer. Ratio 8 : 1. ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 54.0 (CH_2), 121.9 (CH), 122.4 (CH), 123.8 (Cq), 127.06 (CH), 127.16 (2CH), 127.23 (2CH), 127.5 (CH), 128.0 (2CH), 128.5 (2CH), 128.8 (2CH), 129.2 (2CH), 129.3 (CH), 130.8 (CH), 131.9 (CH), 134.4 (Cq), 136.9 (Cq), 138.0 (Cq), 143.1 (Cq), 165.1 (Cq), 170.2 (Cq). IR (film) 3332, 1677 and 1632 cm^{-1}. HRMS calcd for $C_{27}H_{23}N_2O_2$: 407.1754. Found: 407.1752.

N-Benzyl-2-(*N*-benzylbenzamido)-*N*-phenylbenzamide 5o

To a solution of **5n** (205 mg, 0.50 mmol), in dry THF (5 mL), were added NaH (60%, 80 mg, 2 mmol) and benzyl bromide (0.3 mL, 2.51 mmol) and it was stirred overnight at rt under nitrogen. The mixture was partitioned between ethyl acetate and brine, and the aqueous phase was extracted with ethyl acetate. The organic extracts were dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to AcOEt) to yield **5o** (188 mg, 75%). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 4.10 (d, J = 15 Hz, 1H), 5.10–5.30 (m, 2H), 5.97 (d, J = 15 Hz, 1H), 6.54–7.70 (m, 24H). IR (film) 1644 cm^{-1}. HRMS calcd for $C_{34}H_{28}N_2O_2Na$: 519.2043. Found: 519.2044. HPLC 5.42 min.

Attempted synthesis of ethyl 2-(2-[*N*-benzyl-2-iodobenzamido]benzamido)benzoate

A solution of **3i** (200 mg, 0.44 mmol) in thionyl chloride (5 mL) was refluxed for 3 h. The excess of thionyl chloride was removed under reduced pressure and the residue was dissolved in AcOEt (10 mL). The solution was cooled to 0 °C and Et_3N (0.5 mL, 3.59 mmol) and ethyl 2-aminobenzoate (65 µL, 0.44 mmol) were added. The mixture was allowed to warm to rt and stirred overnight. The mixture was partitioned between ethyl acetate and aqueous

$NaHCO_3$ saturated solution, and the aqueous phase was extracted with ethyl acetate. The organic extracts were dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (DCM) to yield 2-(2-iodophenyl)-4*H*-benzo[*d*][1,3]oxazin-4-one **6a** (114 mg, 75%). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 7.24 (ddd, $J = 7.8$, 7.5 and 1.8 Hz, 1H), 7.53 (td, $J = 7.5$ and 1.2 Hz, 1H), 7.63 (td, $J = 7.5$ and 1.2 Hz, 1H), 7.79 (dd, $J = 8.1$ and 1.2 Hz, 1H), 7.89 (td, $J = 7.8$ and 1.8 Hz, 1H), 7.91 (td, $J = 8.1$ and 1.5 Hz, 1H), 8.08 (dd, $J = 7.8$ and 1.2 Hz, 1H), 8.33 (dd, $J = 7.8$ and 1.5 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 94.6 (Cq), 116.9 (Cq), 127.3 (CH), 128.2 (CH), 128.6 (CH), 129.0 (CH), 130.9 (CH), 132.3 (CH), 135.5 (Cq), 136.7 (CH), 141.1 (CH), 146.2 (Cq), 157.8 (Cq), 159.2 (Cq). IR (film) 1764 cm^{-1}. HRMS calcd for $C_{14}H_9NO_2I$: 349.9672. Found: 349.9672. Anal. calcd for $C_{14}H_8NO_2I$ (349.1) C, 48.16; H, 2.31; N, 4.01. Found: C, 48.59; H, 2.30; N, 3.96%. Mp 120–122 °C.

Attempted synthesis of ethyl 2-(2-[*N*-benzyl-1-naphthamido]benzamido)benzoate

A solution of **3g** (468 mg, 1.23 mmol) in thionyl chloride (10 mL) was refluxed for 3 h. The excess of thionyl chloride was removed under reduced pressure and the residue was dissolved in AcOEt (12 mL). The solution was cooled to 0 °C and Et_3N (2.6 mL, 18.6 mmol) and ethyl 2-aminobenzoate (0.18 mL, 1.22 mmol) were added. The mixture was allowed to warm to rt and stirred overnight. The mixture was partitioned between ethyl acetate and aqueous $NaHCO_3$ saturated solution, and the aqueous phase was extracted with ethyl acetate. The organic extracts were dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (DCM) to yield 2-(naphthalen-4-yl)-4*H*-benzo[*d*][1,3]oxazin-4-one **6b** (289 mg, 86%). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 7.53–7.61 (m, 3H), 7.66 (ddd, $J = 8.4$, 6.9 and 1.5 Hz, 1H), 7.79 (dd, $J = 8.1$ and 1.2 Hz, 1H), 7.85 (dd, $J = 6.9$ and 1.5 Hz, 1H), 7.92 (dd, $J = 8.1$ and 1.5 Hz, 1H), 8.04 (d, $J = 8.1$ Hz, 1H), 8.29 (dd, $J = 7.8$ and 1.2 Hz, 1H), 8.31 (dd, $J = 7.5$ and 1.2 Hz, 1H), 9.15 (d, $J = 8.4$ Hz, 1H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 116.8 (Cq), 124.7 (CH), 125.7 (CH), 126.3 (CH), 126.8 (Cq), 127.3 (CH), 127.8 (CH), 128.46 (CH), 128.54 (CH), 128.8 (CH), 130.0 (CH), 130.7 (Cq), 133.1 (CH), 134.0 (Cq), 136.5 (CH), 146.7 (Cq), 157.6 (Cq), 159.7 (Cq). IR (film) 1762 cm^{-1}. HRMS calcd for $C_{18}H_{12}NO_2$: 274.0863. Found: 274.0863. Mp 108–130 °C.

N,*N*′-Di(2-iodobenzoyl)benzene-1,2-diamine 7a

To a solution of 1,2-diaminobenzene (255 mg, 2.36 mmol) and pyridine (1 mL, 12.4 mmol) in DCM (10 mL), was added 2-iodobenzoyl chloride (1.24 g, 4.65 mmol). The mixture was stirred at rt under nitrogen for 24 h. To the resulting suspension petroleum ether was added and the mixture was filtrated to obtain **7a** as an unsoluble solid (1 g, 75%) which was used without further purification. *m*/*z* (ES$^-$) 567 (100%, M–H$^+$).

N,*N*′-Di(2-iodobenzoyl)-*N*,*N*′-dimethylbenzene-1,2-diamine 7b

To a suspension of **7a** (102 mg, 0.18 mmol) in THF (25 mL), was added NaH (60%, 60 mg, 1.5 mmol), and methyl iodide (0.50 mL, 8.04 mmol). The mixture was stirred at rt under nitrogen for 24 h. The residue was partitioned between DCM and water, and the aqueous phase was extracted with DCM. The organic extracts were dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 50%) to yield **7b** (91 mg, 85%). ^{1}H-NMR ($CDCl_3$, 300 MHz) major conformer δ 3.26 (s, 3H), 7.14 (ddd, $J = 7.8$, 7.5 and 1.8 Hz, 2H), 7.33–7.37 (m, 2H), 7.44 (dd, $J = 7.2$ and 0.9 Hz, 2H), 7.46–7.52 (m, 2H), 7.57–7.60 (m, 2H), 7.91 (d, $J = 7.8$ Hz, 2H). Minor conformer δ 3.57 (s, 3H), 6.88 (td, $J = 7.8$ and 1.5 Hz, 2H), 7.04–7.92 (m, 8H, masked by the major conformer), 7.79 (d, $J = 7.8$ Hz, 2H). Ratio 5 : 1. ^{13}C-NMR ($CDCl_3$, 75.5 MHz) δ 39.9 (CH_3), 92.4 (Cq), 126.9 (CH), 128.4 (CH), 129.3 (CH), 130.5 (CH), 130.6 (Cq), 139.5 (CH), 142.1 (Cq), 170.5 (Cq). IR (film) 1649 cm^{-1}. HRMS calcd for $C_{22}H_{19}N_2O_2I_2$: 596.9530. Found: 596.9530. HPLC 5.50 min.

N,*N*′-Dibenzyl-*N*,*N*′-di(2-iodobenzoyl)benzene-1,2-diamine 7c

To a suspension of **7a** (126 mg, 0.22 mmol) in THF (25 mL), were added NaH (60%, 96 mg, 2.4 mmol), and benzyl bromide (0.25 mL, 2.09 mmol). The mixture was stirred at rt under nitrogen for 24 h. The residue was partitioned between DCM and water, and the aqueous phase was extracted with DCM. The organic extracts were dried and filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (petroleum ether to petroleum ether–AcOEt 50%) to yield **7c** (132 mg, 79%). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 4.33–4.97 (m, 4H), 5.95–6.05 (m, 1H), 6.56–7.93 (m, 21H). Complex mixture of conformers. IR (film) 1649 cm^{-1}. HRMS calcd for $C_{34}H_{27}N_2O_2I_2$: 749.0156. Found: 749.0154.

X-Ray crystallography

Data for the X-ray crystal structures described in this paper have been deposited with the Cambridge Crystallographic database.†

3a. Crystal data $C_{20}H_{15}I_2NO$; $M = 539.13$; triclinic *P*-1; $a = 9.0770(8)$ Å; $b = 10.3330(9)$ Å; $c = 10.9250(9)$ Å; $\alpha = 95.4550(10)$; $\beta = 101.4960(10)$; $\gamma = 106.2000(10)$; $V = 951.82(14)$ Å^3; $T = 100(2)$ K; $Z = 2$; $\mu = 3.310$ mm^{-1}; 8260 reflections; $R_{int} = 0.0128$; $R(F)$ 0.0188; CCDC reference number 299474.

3b. Crystal data $C_{20}H_{14}I_3NO$; $M = 665.02$; orthorhombic *Pbcn*; $a = 17.2130(10)$ Å; $b = 14.9120(8)$ Å; $c = 15.6580(9)$ Å; $V = 4019.1(4)$ Å^3; $T = 100(2)$ K; $Z = 8$; $\mu = 4.674$ mm^{-1}; 33041 reflections; $R_{int} = 0.0250$; $R(F)$ 0.0255; CCDC reference number 299475.

7b. Crystal data $C_{22}H_{18}I_2N_2O_2{\cdot}CH_2Cl_2$; $M = 681.11$; monoclinic *P*2(1); $a = 7.984(5)$ Å; $b = 24.878(5)$ Å; $c = 12.520(5)$ Å; $V = 2459.5(19)$ Å^3; $T = 100(2)$ K; $Z = 4$; $\mu = 2.797$ mm^{-1}; 14331 reflections; $R_{int} = 0.0267$; $R(F)$ 0.0411; CCDC reference number 299476.

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