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Conformational studies of tertiary oligo-*m*-benzanilides and oligo-*p*-benzanilides in solution

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ABSTRACT

A series of oligo-*m*- and *p*-benzanilides were made and their conformations in solution were studied by NMR. In most cases, conformational mixtures were observed as soon as three or more monomers were incorporated into the oligomer. Some crystal structures were obtained, which indicated that helical conformations were adopted in the solid state.

1. Introduction

Amide bond structure has been studied extensively, because the amide moiety is one of the most important functions in biological systems.[1] Numerous synthetic *foldamers*,[2] or oligomers with a well-defined conformation, have been described which use the amide or urea linkage to provide stability and rigidity.[3–6] For example, secondary benzanilides **A** generally adopt a rings-trans (formally *Z*) conformation (Fig. 1) and their oligomers have proven to adopt a well-defined helical structure, a consequence of both the preferred geometry of the amide bonds and their hydrogen bonding ability.[4]

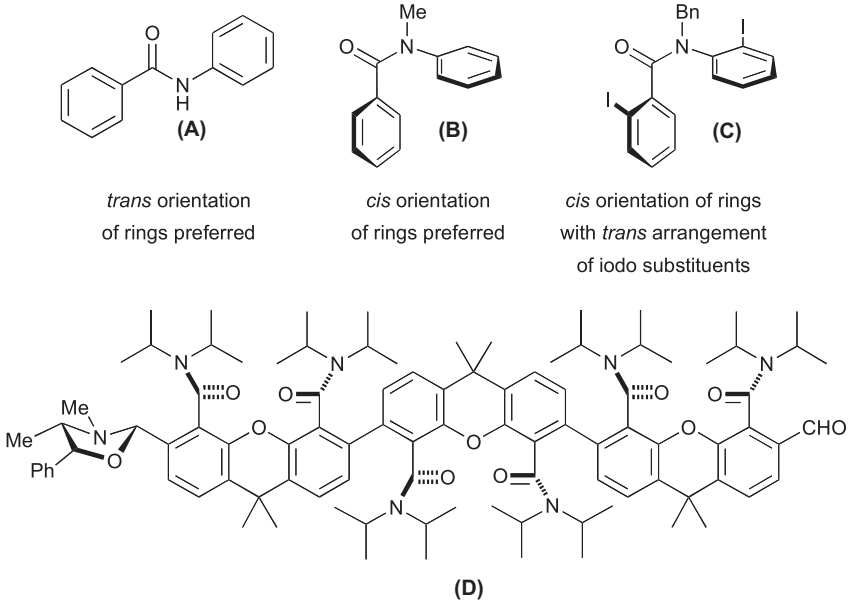

Figure 1. Conformational control in amides.

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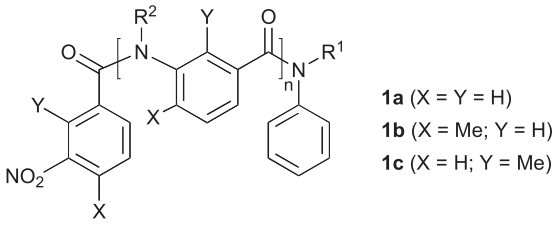
The conformation of *N*-alkylated anilides has also been investigated in detail, and it has been shown that *N*-alkylated benzanilides favour the conformation **B**, which places the aryl rings cis (formally *E*) in the crystal and in solution.[7] The conformational ratio of tertiary benzamides can be altered by the size of substituents at the aromatic *ortho* position and on the nitrogen atom.[8,9] For instance, we showed that benzanilide **C** bearing two iodo substituents at the *ortho* position of each ring and a benzyl group on the nitrogen exhibit high conformational control (10:1).[9] The ability of *N*-alkylated and *para*-linked oligobenzanilides to adopt a secondary helical structure in solution and in the solid state has been studied by Tanatani et al.[10] Crystal data suggested that the helical structures are enforced mainly by the inherent structural propensities of aromatic amide bonds, such as regularity of amide torsion angles, as well as the cis conformation of the amide bonds and the *syn* arrangement of the benzene rings. Wilson has shown that this helical preference can be used to favour a macrocyclisation reaction.[11] A terminal planar chiral residue can control the resulting screw sense of the helical oligomer as judged by circular dichroism.[12] *meta*-Linked benzanilides carrying terminal carboxylic acid functions,[13] and *N*-methyl aromatic amide bearing 2,6-disubstitued pyridines, also adopt a well-defined conformation in solution.[14] An NMR study of related oligo *ortho*-linked oligobenzanilides concluded that conformational communication breaks down once the chain is extended to greater than three monomers, and mixtures of conformers are evident by NMR.[9]

Our interest in the solution structure of oligomeric amides stems for attempts to use them as a scaffold through which stereochemical information might be relayed in the form of conformational changes.[15–20] Thus, we showed that dipole interactions within trisxanthenehexacarboxamide **D** were able to mediate remote asymmetric induction over a total of 23 bond lengths.[15] We recently reported the use of NMR to examine the extent to which oligomeric ureas[6] and peptide-like oligo-Aib amides[21] adopt a helical structure, and in this paper we now report on the conformational behaviour of unsubstituted and substituted oligo(*m*-benzanilides) **1a**–**c** (Fig. 2). We also report preliminary studies on some analogous oligomers, principally those of *p*-aminobenzoic acid. Much of the work made use of low temperature NMR analysis, and it became a significant challenge to establish whether a single set of peaks was due to a single conformer or to sets of rapidly interconverting oligomers in fast exchange. In most cases more extended oligomers frequently showed mixtures of conformers. Our pragmatic aim of identifying well-controlled oligomeric structures meant that the question of whether this is due to a slowing of rotation with greater steric hindrance, or due to a loss of control in more complex systems was in these cases left unanswered.

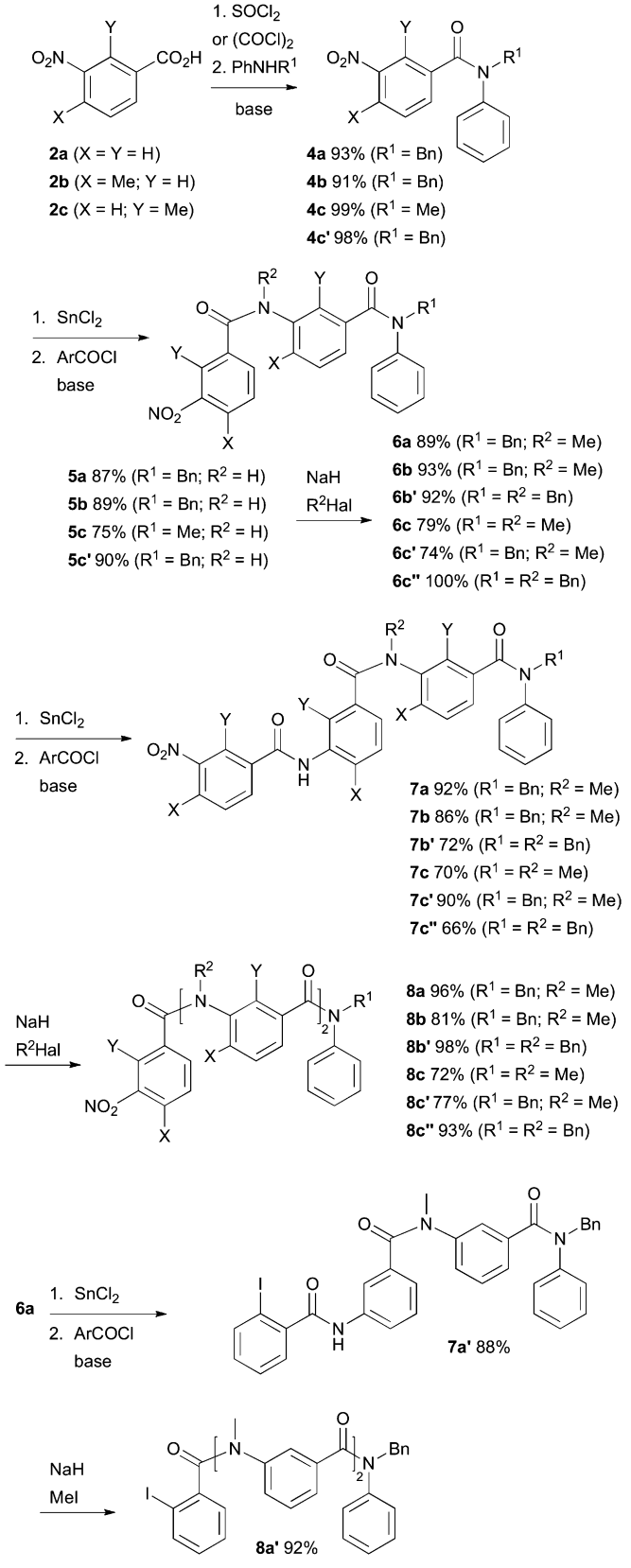


1a (X = Y = H)
1b (X = Me; Y = H)
1c (X = H; Y = Me)

Figure 2. Oligo(*m*-benzanilides) **1a**–**c** (*n*=0–2).

2. Results and discussion

The general approach to the oligomers **1** derived from *m*-aminobenzoic acid is depicted in Scheme 1. The synthesis began with commercially available 3-nitrobenzoic acid or its methylated analogues **2a**–**c**. These were converted into the corresponding acid chlorides using thionyl chloride or oxalyl chloride and condensed with *N*-methylaniline or *N*-benzylaniline under basic conditions (Et_3N or pyridine) to yield monomers **4**. The nitro group was reduced with tin(II)chloride; reaction with a further equivalent of the freshly prepared acid chloride derivative of **2a**–**c** gave the secondary amides **5**.[5] Alkylation was achieved by treating amides **5** with sodium hydride and then quenching with MeI or BnBr to



Scheme 1. Synthesis of oligo(*m*-benzamides).

generate the set of six diamides **6**. The sequence of nitro group reduction, acylation (to give the seven triamides **7**) and alkylation was then repeated to increase the length of oligomers, finally supplying the set of fully alkylated triamides **8**.

2.1. Conformational analysis of oligo-*m*-benzanilides 1a

We first examined the conformational behaviour of simple, unsubstituted oligo(*m*-benzamides) **1a** (R^1=Bn, R^2=Me), exemplified by diamide **6a** and triamide **8a**. A characteristic shift of aromatic protons upfield was evident on alkylation of the secondary amides **5a** and **7a** to yield the tertiary amides **6a** and **8a**, suggesting adoption of a cis amide geometry as expected.[7,8] A simple, well resolved spectrum at 25 °C suggested that **8a** was conformationally uniform about the C–N bond of the amides.[9] However lack of evident diastereotopicity in the geminal CH_2Ph protons of the benzyl group of **6a** or **8a** indicated that if a helical structure was present in solution, the enantiomeric helices were interconverting rapidly on the NMR timescale and therefore not amenable to study by NMR.[6]

Modification was therefore made to the structure of **8a** by ligating **6a** with 2-iodobenzoyl chloride to yield **7a**′ and hence **8a**′ Because of expected slow rotation about the Ar–CO axis of the iodobenzamide unit,[22] we hoped that coupling of the rate of helical inversion with this bond rotation would allow us to detect helicity from evidence of local chirality in the form of the CH_2 signal arising from the terminal *N*-benzyl group of **8a**′. However, at 25 °C and at −60 °C in $CDCl_3$ these signals appeared as a simple 2H singlet. This suggests that **8a**′ is either not helical, or that the *o*-iodophenyl substituent is unable to induce a preferred helicity in **8a**′.

2.2. Conformational analysis of oligo-4-methyl-*m*-benzanilides 1b

Lack of informative data from NMR of **8a**,**a**′ led us to adopt a more stepwise approach to identification of conformational preferences.

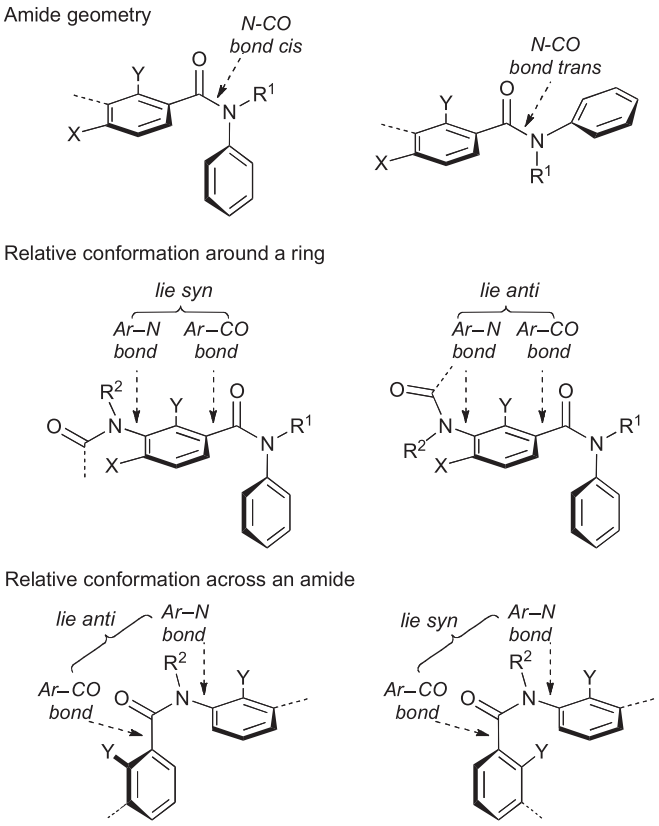


Figure 3. Conformational stereochemical features of **6**–**8**.

Commercially available 4-methyl-3-nitrobenzoic acid was chosen as the starting material for oligomers **1b** (R^1=Bn, exemplified by **6b**, **6b**′, **8b** and **8b**′) with the intention that the additional aromatic

Table 1
Conformational isomerism

	Amide linkages	Possible observable amide N–CO *cis*/*trans* conformers[a]	Possible observable Ar–N and Ar–CO diastereoisomeric conformers[b]	Ratio of conformers evident in NMR[c]
6b	2	4	1	>95:5
6b′	2	4	1[d]	>95:5
7b	3	4	1	90:10
7b′	3	4	1[d]	>95:5
8b	3	8	2	60:30:10
8b′	3	8	2	[e]
6c	2	4	4	80:20
6c′	2	4	4	80:20 88:12 (−60 °C) 82:18 (C_6D_6) 87:13 (THF) 87:13 (DMSO)
6c″	2	4	4	85:15
6d	2	4	2 (or 4)	84:16
6e	2	4	2	>95:5
7c	3	4	4	77:23
7c′	3	4	4	75:25
7c″	3	4	4	83:17
7d	3	4	2 (or 4)	95:5
7e	3	4	2	90:10
8c	3	8	16	[e]
8c′	3	8	16	[e]
8c″	3	8	16	[e]
8d	3	8	4 (or 16)	[e]
8e	3	8	4	[e]

[a] Excluding secondary amides, which always lie *trans*.
[b] On the basis that one 2-substituent is required for the observation of conformers in tertiary benzamides and anilides [Refs. 22–25].
[c] In $CDCl_3$ at 23 °C unless otherwise indicated.
[d] A pair of slowly interconverting enantiomeric conformers indicated by diastereotopicity in the CH_2Ph group.
[e] Complex mixture of conformers.

methyl group *ortho* to the nitrogen atom would slow the rotation about each Ar–N bond to the point that diastereoisomeric conformations would be distinguishable by NMR.[22–24] Figure 3 shows conformational possibilities available to these and related structures, and Table 1 includes an analysis of the likely number of conformers available to each oligomer studied, along with the conformational ratio actually observed by ^{1}H NMR at ambient temperature or below. In **1b** however the Ar–CO bonds in such structures remain unencumbered by *ortho* substituents and so are unable to give rise to distinguishable Ar–CO conformers.[25] The ^{1}H NMR spectrum in $CDCl_3$ at rt suggested that compound **5b** exists as a single conformer with regard to the N–CO bonds (presumably the secondary amide being trans and the tertiary being cis).[7,8] N-Alkylation using methyl iodide or benzyl bromide gave the diamides **6b** and **6b′**, respectively again as single (presumably cis,cis) N–CO conformers by NMR. Interestingly, these compounds displayed diastereotopic benzylic protons as a result of the slow rotation (on the NMR timescale) about the Ar–N bond. In contrast, the benzylic protons of amide **5b** are not diastereotopic, because rotation about the Ar–N bond of a secondary anilide is fast on the NMR timescale.[26]

Addition of the third residue created the triamides **7b** and **7b′** (entries 6 and 7). Although **7b′** appeared as one conformer in solution, a small amount of a second conformer (in which a clearly deshielded aromatic proton was observable) was evident in **7b**, presumably arising from population of the trans conformer of the tertiary amide, now that the *cis* amide bond has become significantly more hindered.[8,9]

After alkylation, trimers **8b** and **8b′** clearly existed as a mixture of conformers in $CDCl_3$ at 25 °C. Although it was not possible to determine the ratio of conformers of the *N*-benzylated trimer **8b′**, we quantified the ratio of the three conformers of **8b** evident in the ^{1}H NMR spectrum at 25 °C as 60:30:10. The significant new feature possessed by **8b** is the possibility of *syn*/*anti* diastereoisomeric conformers arising from two slowly rotating Ar–N bonds: we assumed that population of both of these alternatives gives rise to the 2:1 ratio, while the further minor conformer represents population of the *trans* N–CO isomer of the amide.

2.3. Conformational analysis of oligo-2-methyl-*m*-benzanilide 1c

Oligomers **1c** (represented by **6c**–**c″** and **8c**–**c″**) in which a methyl group intervenes between the Ar–N and Ar–CO bond were investigated. Slowing of rotation about both bonds potentially gives rise to a *syn*/*anti* pair of conformers for each aromatic residue in the oligoamide, and thus provides a stringent test of whether conformation is being controlled in the solution state. The overall yield and conformational ratios of the monomers and dimers are listed in Table 1.

As before, fast conformational exchange means that diamides **5c**–**c′** having a secondary amide exhibit a sharp, clean spectrum. After alkylation, the tertiary diamides **6c**–**c″** were however present in solution as a mixture of two major conformers in a ratio of 4:1 to 7.5:1 depending on solvent and temperature. In some cases, additional minor conformers were also detectable by ^{1}H NMR but could not be quantified. All three diamides **6c**–**c″** were found to have broadened ^{1}H NMR signals at 25 °C, with diastereotopic benzylic protons providing evidence of slow rotation on the NMR timescale about the Ar–CO and/or Ar–N bonds. The results revealed that the size of the R^1 group (=Me or Bn) has virtually no influence on the conformational selectivity (compare **6c**, **6c′**). However, the selectivity slightly increases when R^2 is increased in size from Me to Bn (cf. **6c′**, **6c″**). At low temperature (−60 °C, $CDCl_3$), ^{1}H NMR shows an improvement of conformational ratio to 88:12, but with signals still remaining broadened. Solvent effects on the conformational ratio of **6c′** were also studied at 25 °C, with marginally better conformational selectivities obtained in C_6D_6 (82:18), THF-d_8 (87:13) and DMSO-d_6 (87:13).

2.4. Detailed analysis of 6c′

Although disappointingly not conformationally uniform, the fact that only two conformers appear to predominate in compound **6c′** with the potential to exhibit (on the NMR timescale) four geometrical (*cis*/*trans*) amide conformers multiplied by four axial (*syn*/*syn*, *syn*/*anti* etc.) conformers (Fig. 4) was remarkable. We were unable to determine directly which of the conformers is this principal component in solution, although X-ray crystallography[27] allowed us to determine the solid state structure of **6c′** (Fig. 5).

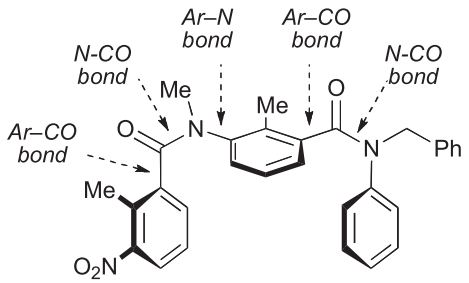


Figure 4. Conformer possibilities in **6c′**.

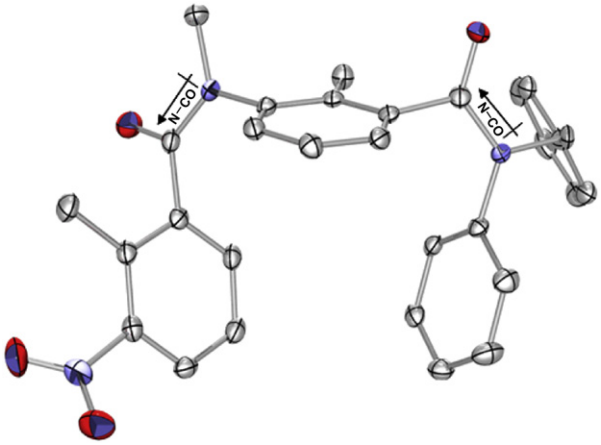
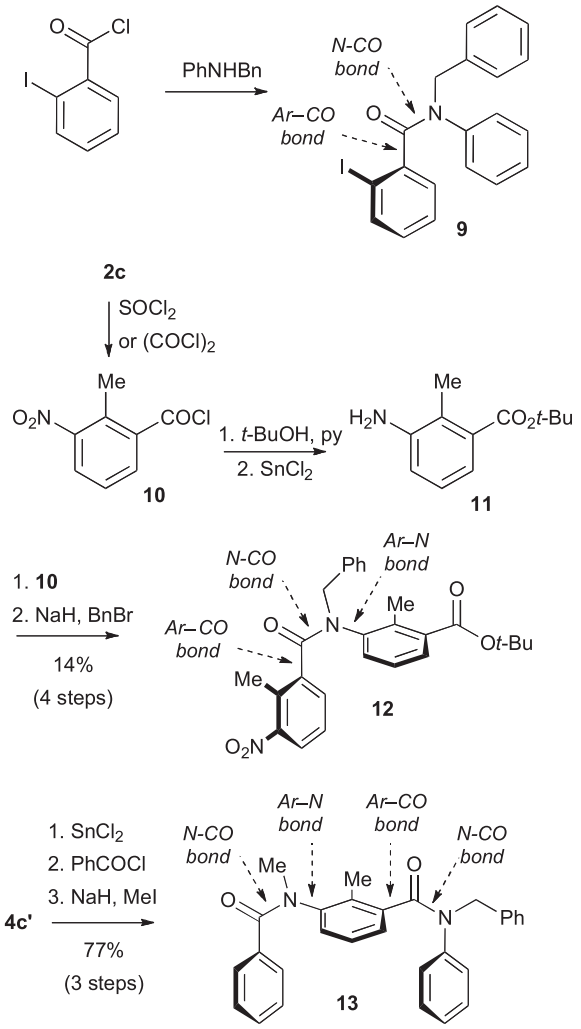


Figure 5. X-ray crystal structure of **6c′**.

Both amide bonds adopt a *cis* C–N conformation, in line with precedent, and as we have previously observed, methyl groups on each aromatic ring flanking the benzanilide amide function are aligned *anti* to avoid steric interaction.[9] The *cis* orientation of benzamides across the central aromatic ring can be explained by a dipole–dipole interaction (shown in Fig. 5) between both amide functions.[28] Unfortunately, we were unable to determine whether the conformation in the solid state is the same as the major conformation in solution—dissolving a crystal of **6c′** at low temperature (−50 °C) and acquiring a ^{1}H NMR spectrum immediately returned the same mixture of conformers as that obtained on cooling a rt solution.

In an attempt to establish which of the conformational features of **6c′** are well controlled, and hence identify the second, minor, conformer, we made analogues of **6c′** lacking one or more of the conformationally restricted amide N–CO, Ar–CO or Ar–N bonds. Compounds **9**, **12** and **13** were made by the methods shown in Scheme 2.

The ^{1}H NMR spectrum of **9** was revealing: it showed two conformers in a ratio of 90:10, which must be rotamers about the N–CO



Scheme 2. Synthesis and conformation of **9**, **12** and **13**.

bond (Fig. 6). The CH_2Ph group of minor rotamer appeared as a sharp AB system (due to slow Ar–CO rotation) at ambient temperature. However, the CH_2Ph group of the major conformer was a broadened singlet at rt, which decoalesced to an AB system on cooling to −50 °C in $CDCl_3$. By variable temperature NMR, modelling the resulting lineshapes, and fitting the rates obtained to the Eyring equation (see Supplementary data) we obtained a barrier to rotation about the Ar–CO bond in the major (rings-cis) conformer of 50.1 kJ mol^{-1} at 25 °C. The corresponding barrier to rotation in the minor (rings-trans) conformer was 62.6 kJ mol^{-1} at 25 °C; interestingly this also shows that N–CO rotation must be slow, or otherwise a stepwise mechanism for Ar–CO bond rotation of the minor conformer would exist by interconversion with the major conformer.

The major conformer of **9**, which presumably has the two aryl rings cis about the N–CO bond as illustrated in Figure 6, has an Ar–CO barrier too low to exhibit rotamers (enantiomeric in this case) at rt, even with a large 2-iodo substituent. This presumably reflects the small size of the N–Ph group, an effect, which has not been studied in detail before.[22] It seemed possible that the apparent conformational uniformity of **6c′** is likewise due to fast Ar–CO bond rotation, although the fact that little change in the ratio of conformers is seen on lowering the temperature to −60 °C suggests this is unlikely.

Amide **12**, which possesses the possibility of cis/trans isomerism and also possibly *syn*/*anti* isomerism about a single N–CO bond shows at 25 °C only one conformer in the ^{1}H NMR spectrum, a result in accordance with previous work on 2,2′-disubstituted benzanilides.[9] Low temperature (−65 °C) NMR spectra of **12** however showed much more complex behaviour, with at least four or five conformers evident. We assume that, as in **9**, this may be due to Ar–CO rotamers becoming spectroscopically distinguishable only at low temperature, and these spectra were not analysed further.

Compound **13** has the possibility of *syn*/*anti* conformational isomerism, along with the possibility of *cis*/*trans* isomerism about two amide bonds. At rt, only a single set of peaks is again observed, but at temperatures below −50 °C, four sets of signals arise in ratio of 69:18:7:6. We assume that the major conformers (which both have downfield benzylic CH_2 protons) arise from *syn*/*anti* isomerism, as before with a barrier to Ar–CO rotation too low to allow these diastereoisomeric structures to be distinguishable at ambient temperature. The minor conformers (one of which has an upfield CH_2 group) are presumably due to cis/trans isomerism.

2.5. Extending the oligomers: 7c–c″, 8c–c″

Although mixtures of conformers were observed for **6** in solution, we decided to extend the investigation to triamides **7c**–**c″**, **8c**–**c″**. These were made as before by reduction, amide formation and alkylation (Scheme 1). Addition of a secondary amide group, expected to adopt a trans conformation and to show fast Ar–CO rotation, introduces no new conformational complexity to these compounds, and indeed the conformational ratio of secondary amides **7c**–**c″** (Table 1) is about the same as that of dimers **6c**–**c′**. However, on alkylation, the possibility of further *cis*/*trans* isomerism and of slow Ar–CO rotation arises, and the ^{1}H NMR spectrum of fully alkylated compounds **8c**–**c″** indicates that these tertiary triamides exist as a mixture of at least four NMR-distinguishable conformers at 25 °C in $CDCl_3$, whatever the size of the nitrogen substituents.

2.6. Hybrid *meta*- and *ortho*- or *para*-substituted aromatic amides

In view of the low conformational control in diamides **6c**–**c″** and triamides **8c**–**c″** we decided to modify the substitution pattern of the oligomers. It appeared that while some conformational control was evident in the diamides, control breaks down in triamides **8c**–**c″**.

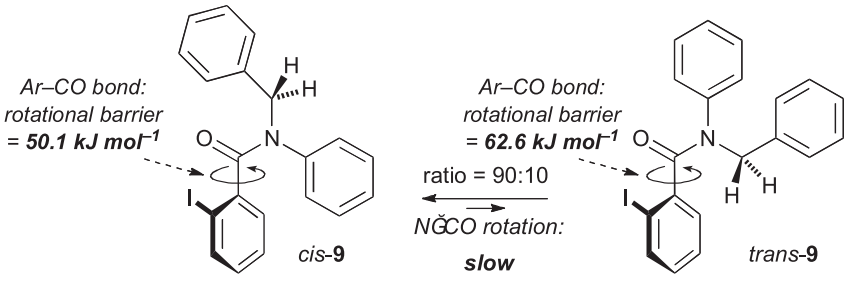
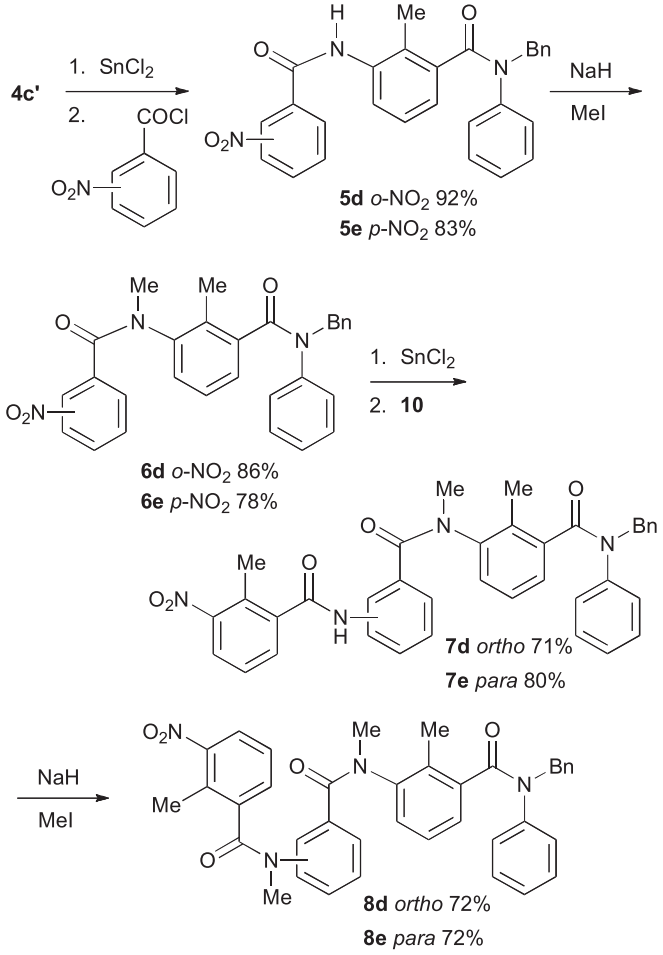


Figure 6. Barriers to bond rotation in **9**.

Thus, we decided to investigate the effect on the selectivity of the substitution pattern of the second benzamide ring. We had already studied the control evident in compounds with a benzamide Ar–CO and an anilide Ar–N axis arranged *ortho* on a single ring.[9] Compounds **7d**, **e** and **8d**, **e** were made by standard methods as shown in Scheme 3.

Benzamides **5d**–**e** appear one conformer in solution by ^{1}H NMR at 23 °C in $CDCl_3$ and display no diastereotopic benzylic protons. Alkylation of **5d** led to **6d**, which appears to exists as an 84:16 mixture of conformers ($CDCl_3$, 25 °C) much like the related structures **6c**–**c″** having an *ortho*-methyl group. By contrast, compound **6e** displays only one set of peaks by ^{1}H NMR at ambient temperature in solution.



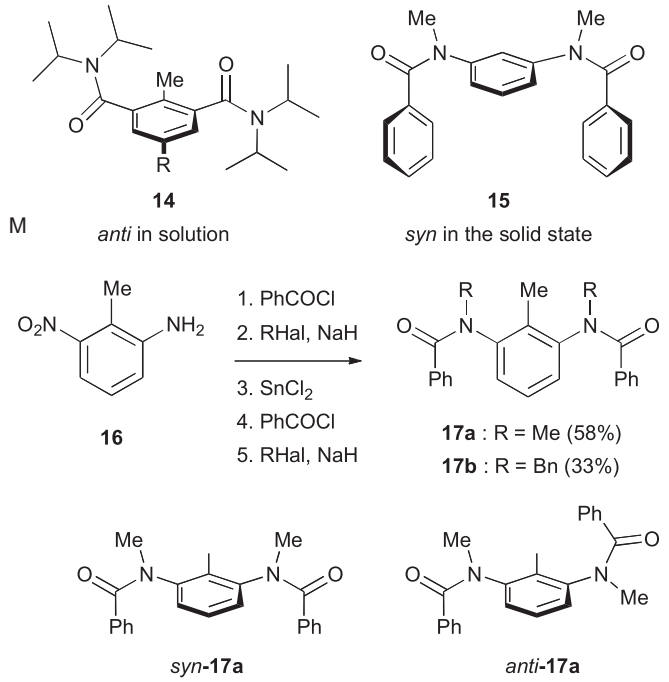
Scheme 3. Synthesis of hybrid *meta* and *ortho*- or *para*-substituted benzanilides.

Trimer **8d** bearing an *ortho*-substituted benzamide was then synthesized. A mixture of several conformers was identified by ^{1}H NMR, presumably due to poor conformational control through the *ortho*-benzamide, as we previously observed for related compounds.[9] ^{1}H NMR of **8e** at 25 °C in $CDCl_3$ was uninformative: a mixture of broad peaks was evident, and low temperature NMR at −60 °C failed to clarify the situation.

2.7. Oligomers from *m*-diaminobenzene and *m*-benzenedicarboxylic acid

We have reported that tertiary benzene-1,3-dicarboxamides **14** with a methyl substituent interposed between the amides adopt an *anti* orientation, driven by dipole interaction.[28] Shudo et al. have studied the conformation in solution and solid state of *N*,*N*′-dimethylisophthalic dianilide **15**, and found that it exists in the *syn* conformation, with *N*-phenyl groups located on the same side of the aromatic ring.[29] In solution, two major conformers were observed arising from the *syn*/*anti* relationship along the benzene ring. Shudo also investigated the conformational behaviour of 1,2-bis(*N*-benzoyl-*N*-methylamino)benzene.[30] This compound displays broad ^{1}H NMR signals at rt, but exists as a mixture of seven conformers in solution at −88 °C (CD_2Cl_2) with the *anti* (along the aromatic ring), *cis*/*cis* (amide) predominating.

We hoped to combine these two *meta*-substituted units into oligomers containing alternating *meta*-phenylenediamine and isophathalic acid units, and as a preliminary to this we made the two amides **17a** and **17b** (Scheme 4). Although in this particular example the final compounds are symmetrical, we used 2-methyl-3-nitrobenzenamine **16** as a precursor that would offer the opportunity to obtain non symmetrical oligomers.



Scheme 4. Synthesis and conformational studies of *meta*-diamidobenzene.

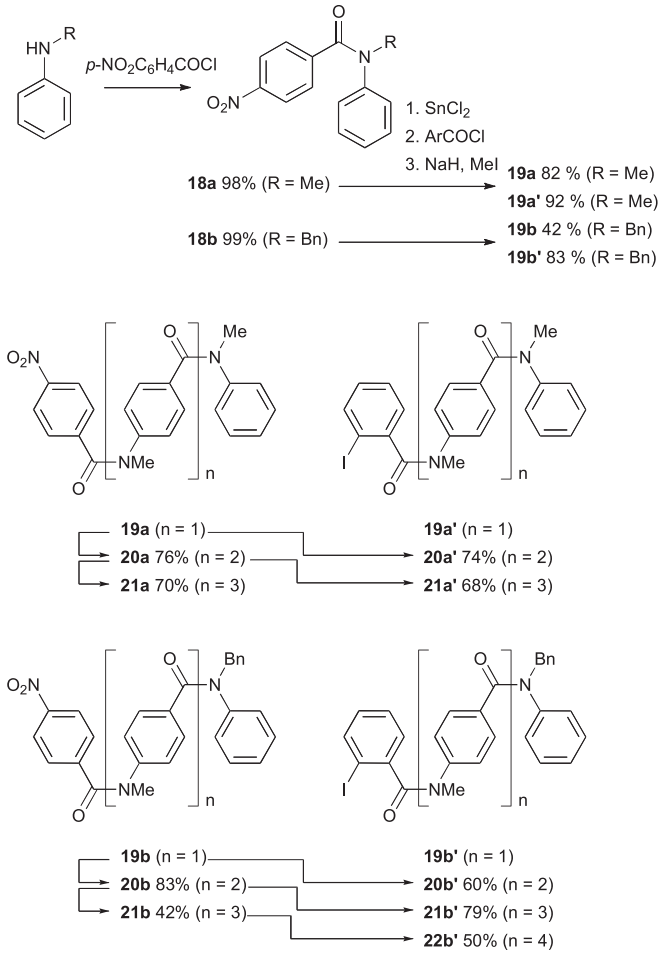
Unfortunately, at 25 °C in $CDCl_3$ a mixture of two conformers was observed for both **17a** and **17b** in a 2:1 ratio. Proton NMR suggests that both amides have *cis* geometry, so the conformers probably arise from *syn* and *anti* isomerism at the central aromatic ring. In light of these results, we did not extend this investigation to oligomers.

2.8. More extended substituted oligo-*m*-benzamides

Although it seemed at this stage that increasing the number of conformationally labile bonds was simply allowing more conformers to be populated, it seemed possible that order would be regained once a helical global secondary structure could be obtained: chain-length dependence is a common feature of foldamer properties. We therefore increased the length of the oligomer to encourage the molecule to fold into a well-defined structure, and exist mainly as one conformer in solution. Unfortunately, the pentamer (**1c**, R^1=Bn, R^2=Me, n=3) and hexamer (**1c**, R^1=Bn, R^2=Me, n=4) were still a mixture of conformers in solution at 25 °C ($CDCl_3$).

2.9. Conformational studies of oligo-*p*-benzanilides

To test whether evidence of helicity in oligo-*p*-benzanilides[10,11] could be detected by diastereotopicity in a terminal CH_2Ph group we constructed oligomers **19**–**22** by a similar route (Scheme 5).



Scheme 5. Synthesis of unsubstituted oligo-*p*-benzanilides.

As with the *m*-benzanilides, in no case we were able to observe anything other than a 2H singlet for the CH_2 groups of **19b′**–**22b′** in a variety of solvents even down to −85 °C. However, we were able to obtain crystal structures of **19a′**[31] and **20a′**[32] and both compounds showed evidence of helicity in the solid state (Figs. 7 and 8). Compound **19a′** is not long enough to generate a full turn of a helix but the X-ray suggests the beginning of a helical conformation. **20a′** is long enough to generate more than one turn in what seems to be more clearly a helix.

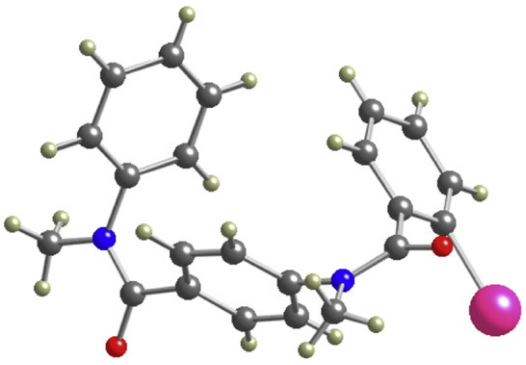


Figure 7. X-ray crystal structure of **19a′**.

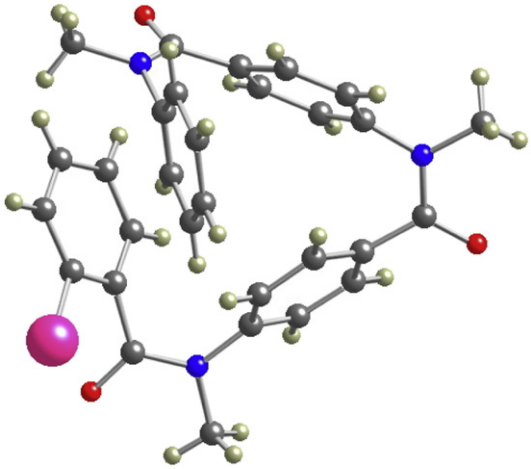


Figure 8. X-ray crystal structure of **20a′**.

After we had carried out this work, a report detailed circular dichroism studies, which indicate that simple oligo-*p*-benzamides, when capped with an enantiomerically pure ferrocenyl unit, adopt helical conformations in solution.[12] However, our method, based on observation of anisochronicity at diastereotopic methylene groups, reports on the local chirality at the terminus of the potential helix, and is therefore more sensitive than simple CD to helix breakdown.

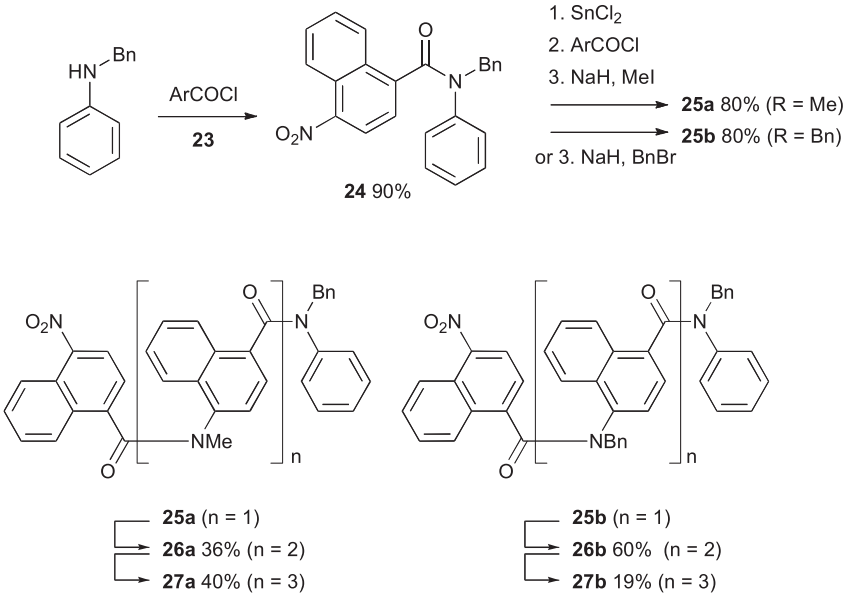
2.10. Oligo-1,4-naphthanilides

Having seen evidence of helicity in oligo-*p*-benzanilides in the solid state, we finally turned to more hindered analogues of these compounds with the aim of slowing individual rotations to the point where detailed conformational selectivity in solution could be quantified. Oligo-1,4-naphthanilides were built by a similar strategy of iterative amide formation with 4-nitronaphthalene-1-carbonyl chloride **23**,[33] reduction and alkylation was used to build oligomers **27a** and **27b**. Scheme 6 shows the compounds made for this work.

Despite the presence of an Ar–CO bond likely to rotate slowly on the NMR timescale,[22,23] no diastereotopic peaks were observed for **24**. However, in **25a** and **25b** diastereotopic peaks were observed, which failed to coalesce at +50 °C in $CDCl_3$. This result is consistent with either a good level of conformational control at the potentially slowly rotating bonds in **25**, or with unexpectedly fast rotation in the Ar–CO bonds but not the Ar–N bond. The latter possibility was tested by lowering the temperature to −75 °C and running a spectrum in toluene—no further decoalescences were observed, so we seem to be attaining good conformational control. However, when further tertiary amide units were added, to give **26** and **27**, complex mixtures of conformers were observed in the NMR spectra at ambient temperature, and no further work was carried out on these oligomers.

3. Conclusion

Building on conformational preferences evident in the solid state, we studied the conformations adopted in solution by a series of oligo-*m*-benzanilides and oligo-*p*-benzanilides hoping to observe limited conformational freedom and may be the formation of helical structures. In the case of short dimers and trimers, some degree of conformational control could be deduced from the simplicity of the ^1H NMR spectra. However, invariably the degree of control degraded significantly as the oligomers were extended further. The best performing of this wider class of non-hydrogen bonded amide-type oligoarenes have turned out to be ureas derived from oligo-*m*-phenylenediamine;[5,6,18] none of the amides presented here appear to have the same degree of more extended control as those ureas.



Scheme 6. Synthesis of oligo-1,4-naphthanilides.

4. Experimental

4.1. General procedure A: amide bond formation

A solution of acid (1 equiv) in dry CH_2Cl_2 (18 mL/mmol) was cooled to 0 °C. Oxalyl chloride (5 equiv) and one drop of DMF were added. The solution was stirred for 3 h at rt. The solvent was removed under reduced pressure. The resulting acid chloride or commercially available acid chloride was dissolved in dry CH_2Cl_2 (5 mL/mmol acid). A solution of amine (2 equiv) and base (Et_3N or pyridine) (2 equiv) in dry CH_2Cl_2 (5 mL/mmol acid) was added at 0 °C. The mixture was stirred at rt overnight. The organic layer was washed with saturated NH_4Cl and brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude mixture purified on silica gel to afford the amide.

4.2. General procedure B: reduction of nitroarenes

$SnCl_2\cdot 2H_2O$ (5 equiv) was added to a solution of nitro aryl (1 equiv) in EtOAc ([$SnCl_2$]=1 M). The mixture was stirred at rt overnight. The solution was then washed with 2 M NaOH solution and the aqueous layer was extracted with EtOAc (×3). The combined organic layers were washed with water, brine and dried over Na_2SO_4. The crude mixture was purified by flash chromatography on silica gel.

4.3. General procedure C: amide alkylation

A solution of amide (1 equiv) in dry THF (9 mL/mmol amide) was added dropwise at 0 °C to a suspension of NaH (60%, 2 equiv) in dry THF (4 mL/mmol NaH). The solution was stirred for 15 min at 0 °C and methyl iodide or benzyl bromide (2 equiv) was added. The resulting solution was stirred at rt for 3 h (or at 0 °C with a *p*-nitrobenzamide substrate, to avoid hydrolysis). After addition of water, the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine and dried over Na_2SO_4. The crude mixture was purified by flash chromatography on silica gel.

*4.3.1. N-Benzyl-N-phenyl-3-nitrobenzamide **4a**.* Prepared according to general procedure A from 3-nitrobenzoylchloride (1.42 g, 7.65 mmol), benzylaniline (1.40 g, 7.65 mmol) and pyridine (2 mL, 25.2 mmol). The crude mixture was purified on silica gel (PE/EtOAc: 8/2) to afford a colourless solid (*m*=2.36 g, 93%). IR (film) 1648, 1528 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 5.18 (s, 2H), 6.96 (dd, *J*=7.9, 1.6 Hz, 2H), 7.11–7.25 (m, 3H), 7.25–7.42 (m, 6H), 7.68 (m, 1H), 8.11 (ddd, *J*=8.2, 2.3, 1.1 Hz, 1H), 8.22 (t, *J*=1.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 54.3 (CH_2), 124.2 (CH), 124.6 (CH), 127.2 (CH), 127.9 (CH), 128.3 (CH), 128.9 (CH), 128.9 (CH), 129.2 (CH), 129.7 (CH), 134.7 (CH), 136.6 (Cq), 137.9 (Cq), 142.7 (Cq), 147.8 (Cq), 168.2 (Cq). MS (ESI^+) *m*/*z*: 333 (67) [M+H]. HRMS calcd for $C_{20}H_{17}N_2O_3$: 333.1234, found: 333.1233.

*4.3.2. N-(N′-Benzyl-N′-phenyl-3-carboxamidophenyl)-3-nitrobenzamide **5a**.* Prepared according to general procedure B from nitro compound **4a** (1.10 g, 3.31 mmol) and $SnCl_2\cdot 2H_2O$ (7.70 g, 34.1 mmol). The amine was obtained without further purification as a clear, foamy solid (*m*=930 mg, 93%). IR (film) 3355, 1633, 1495 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 3.48 (br s, 2H), 5.15 (s, 2H), 6.56 (ddd, *J*=7.9, 2.4, 0.8 Hz, 2H), 6.64 (d, *J*=7.7 Hz, 1H), 6.80 (m, 1H), 6.91 (t, *J*=7.6 Hz, 1H), 6.96 (m, 1H), 7.09–7.21 (m, 3H), 7.26–7.37 (m, 5H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 54.1 (CH_2), 115.9 (CH), 116.6 (CH), 119.2 (CH), 126.9 (CH), 127.6 (CH), 127.8 (CH), 128.6 (CH), 128.7 (CH), 129.2 (CH), 137.3 (Cq), 137.9 (Cq), 143.9 (Cq), 146.4 (Cq), 171.1 (Cq). MS *m*/*z* (ESI^+): 303 (100) [M+H]. HRMS calcd for $C_{20}H_{19}N_2O$: 303.1492, found: 303.1489. Mp=117–119 °C.

The amine was used to make the amide **5a** by general procedure A using amine (800 mg, 2.65 mmol), 3-nitrobenzoylchloride (490 mg, 2.65 mmol) and pyridine (0.71 mL, 8.75 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 8/2) to afford a creamy foam (*m*=1.12 g, 94%). IR (film) 1623, 1595, 1527 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 5.06 (s, 2H), 6.85–7.02 (m, 3H), 7.03–7.33 (m, 9H), 7.61 (t, *J*=7.9, 7.9 Hz, 1H), 7.79 (s, 1H), 7.93 (d, *J*=8.3 Hz, 1H), 8.28 (d, *J*=7.6 Hz, 1H), 8.35 (dd, *J*=8.1, 1.4 Hz, 1H), 8.77 (s, 1H), 9.47 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 54.2 (CH_2), 120.6 (CH), 122.2 (CH), 122.6 (CH), 124.4 (CH), 126.4 (CH), 127.4 (CH), 127.8 (CH), 128.1 (CH), 128.5 (CH), 128.6 (CH), 128.8 (CH), 129.4 (CH), 129.9 (CH), 134.2 (CH), 136.7 (Cq), 136.8 (Cq), 137.1 (Cq), 138.5 (Cq), 142.8 (Cq), 148.3 (Cq), 163.9 (Cq), 171.1 (Cq). MS *m*/*z* (ESI^-): 450 (100) [M−H]. HRMS calcd for $C_{27}H_{19}N_3O_4$: 466.1761, found: 452.1607. Mp=143–145 °C.

*4.3.3. N-(N′-Benzyl-N′-phenyl-3′-carboxamidophenyl)-N-methyl-3-nitrobenzamide **6a**.* Prepared according to general procedure C

from amide **5a** (300 mg, 0.665 mmol), NaH (64.0 mg, 1.60 mmol) and iodomethane (0.42 mL, 6.75 mmol). The crude mixture was purified through silica gel (DCM then DCM/MeOH: 100/3) to afford a creamy solid (m=277 mg, 89%). IR (film) 1647, 1521 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 3.17 (s, 3H), 5.00 (s, 2H), 6.70–6.92 (m, 4H), 6.93–7.28 (m, 12H), 7.95 (d, J=7.8 Hz, 1H), 8.10 (s, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 38.3 (CH_3), 54.2 (CH_2), 124.2 (CH), 124.7 (CH), 127.2 (CH), 127.4 (CH), 127.8 (CH), 127.8 (CH), 128.1 (CH), 128.6 (CH), 128.8 (CH), 128. 9 (CH), 129.2 (CH), 129.3 (CH), 129.5 (CH), 134.6 (CH), 137.2 (Cq), 137.4 (Cq), 137.7 (Cq), 143.1 (Cq), 143.7 (Cq), 147.8 (Cq), 167.9 (Cq), 169.2 (Cq). MS m/z (ESI^+): 466 (22) [M+H]. HRMS calcd for $C_{28}H_{24}N_3O_4$: 466.1605, found: 466.1761.

4.3.4. N-(N′-(N″-Benzyl-N″-phenyl-3″-carboxamidophenyl)-N′-methyl-3′-carboxamidophenyl)-3-nitrobenzamide ***7a****.* Prepared according to general procedure B from nitro compound **6a** (318 mg, 0.684 mmol) and $SnCl_2\cdot 2H_2O$ (1.58 g, 7.00 mmol). The title compound was obtained without further purification as a creamy foam (m=281 mg, 95%). IR (film) 3353, 1632, 1496 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 3.25 (s, 3H), 3.41 (br s, 2H), 5.14 (s, 2H), 6.31 (d, J=7.5 Hz, 1H), 6.57 (ddd, J=8.0, 2.4, 0.9 Hz, 1H), 6.72 (t, J=1.8 Hz, 1H), 6.77–6.91 (m, 4H), 6.99 (t, J=7.9 Hz, 1H), 7.10–7.24 (m, 5H), 7.24–7.39 (m, 5H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 38.3 (CH_3), 54.1 (CH_2), 115.6 (CH), 116.6 (CH), 119.2 (CH), 126.9 (CH), 126.9 (CH), 127.2 (CH), 127.8 (CH), 128.1 (CH), 128.6 (CH), 128.7 (CH), 128.7 (CH), 128.7 (CH), 128.8 (CH), 129.4 (CH), 136.8 (Cq), 137.3 (Cq), 137.4 (Cq), 143.6 (Cq), 144.7 (Cq), 146.3 (Cq), 169.7 (Cq), 170.9 (Cq). MS m/z (ESI^+): 436 (47) [M+H]. HRMS calcd for $C_{28}H_{26}N_3O_2$: 436.2020, found: 436.2019. Mp=102–106 °C.

The amine was used to make the title compound according to general procedure A using amine (100 mg, 0.229 mmol), 3-nitrobenzoylchloride (300 mg, 2.30 mmol) and pyridine (0.6 mL, 7.59 mmol). The crude mixture was purified through silica gel (DCM to DCM/MeOH: 100/3) to afford a white, foamy solid (m=130 mg, 97%). IR (film) 1624, 1596, 1525 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 3.20 (s, 3H), 5.10 (s, 2H), 6.58 (d, J=7.7 Hz, 1H), 6.87 (dd, J=7.9, 1.4 Hz, 3H), 6.98 (dt, J=7.8, 5.1 Hz, 2H), 7.06–7.31 (m, 9H), 7.55–7.72 (m, 3H), 7.95 (dd, J=8.2, 1.2 Hz, 1H), 8.24–8.29 (m, 1H), 8.35 (ddd, J=8.3, 2.2, 1.0 Hz, 1H), 8.71 (t, J=1.8 Hz, 1H), 9.66 (s, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 38.3 (CH_3), 54.2 (CH_2), 120.8 (CH), 122.1 (CH), 122.6 (CH), 124.4 (CH), 126.3 (CH), 127.1 (CH), 127.2 (CH), 127.3 (CH), 127.7 (CH), 128.1 (CH), 128.6 (CH), 128.7 (CH), 128.9 (CH), 129.4 (CH), 129.9 (CH), 134.3 (CH), 136.1 (CH), 136.7 (Cq), 137.1 (Cq), 134.4 (Cq), 137.4 (Cq), 138.6 (Cq), 143.1 (Cq), 144.0 (Cq), 148.2 (Cq), 163.9 (Cq), 169.8 (Cq), 170.7 (Cq). MS m/z (ESI^+): 585 (33) [M+H]. HRMS calcd for $C_{36}H_{30}IN_3NaO_3$: 585.2132, found: 585.2144. Mp=151–153 °C.

4.3.5. N-(N′-(N″-Benzyl-N″-phenyl-3″-carboxamidophenyl)-N′-methyl-3′-carboxamidophenyl)-2-iodobenzamide ***7a′****.* Prepared according to general procedure A from amine derived from **6a** (263 mg, 0.600 mmol), iodobenzoylchloride (160 mg, 0.601 mmol) and pyridine (0.24 mL, 1.98 mmol). The crude mixture was purified through silica gel (3% MeOH/DCM) to afford a beige foamy solid (m=351 mg, 88%). ^1H NMR ($CDCl_3$, 300 MHz) δ ppm 9.17 (s, 1H), 7.92 (d, J=7.7 Hz, 1H), 7.82 (d, J=8.0 Hz, 1H), 7.68 (s, 1H), 7.40–7.04 (m, 13H), 6.98 (q, J=8.0, 7.9, 7.9 Hz, 1H), 6.85 (d, J=6.9 Hz, 2H), 6.76 (d, J=7.7 Hz, 3H), 6.53 (d, J=7.5 Hz, 1H), 5.07 (s, 1H), 3.01 (s, 3H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ ppm 38.4, 53.9, 120.9, 121.9, 124.3, 126.9, 127.2, 127.4, 127.8, 128.0, 128.1, 128.2, 128.4, 128.6, 129.0, 129.5, 131.4, 132.6, 132.9, 134.5, 135.3, 135.9, 137.3, 137.3, 138.7, 139.9, 141.5, 142.4, 143.2, 144.2, 161.5, 168.0, 168.3, 169.7, 170.4. MS m/z (ESI^+) 689 (23%). HRMS calcd for $C_{35}H_{28}I\ N_3NaO_3$: 688.1068, found: 688.1065. Mp 123–125 °C.

4.3.6. N-(N′-(N″-Benzyl-N″-phenyl-3″-carboxamidophenyl)-N′-methyl-3′-carboxamidophenyl)-N-methyl-3-nitrobenzamide ***8a****.* Prepared according to general procedure C from amide **7a** (84.0 mg, 0.144 mmol), NaH (6.00 mg, 0.150 mmol) and iodomethane (0.09 mL, 1.44 mmol). The crude mixture was purified through silica gel (DCM then DCM/MeOH: 100/3) to afford a white solid (m=86 mg, 96%). IR (film) 1644, 1602 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 3.20 (s, 3H), 3.40 (s, 3H), 5.15 (s, 2H), 6.54 (d, J=8.0 Hz, 1H), 6.74 (d, J=7.6 Hz, 1H), 6.84–7.02 (m, 5H), 7.07–7.51 (m, 13H), 8.14 (dd, J=10.5, 2.3 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 38.6 (CH_3), 38.6 (CH_3), 54.3 (CH_2), 124.2 (CH), 124.7 (CH), 126.8 (CH), 127.4 (CH), 127.5 (CH), 127.6 (CH), 127.7 (CH), 127.9 (CH), 128.2 (CH), 128.8 (CH), 128.8 (CH), 128.9 (CH), 129.0 (CH), 129.4 (CH), 129.5 (CH), 134.7 (Cq), 137.3 (Cq), 137.4 (Cq), 137.8 (Cq), 143.4 (Cq), 144.0 (Cq), 144.1 (Cq), 147.8 (Cq), 168.0 (Cq), 168.9 (Cq), 169.2 (Cq). MS m/z (ESI^+) 621 (47) [M+Na]. HRMS calcd for $C_{36}H_{30}N_4NaO_5$: 621.2108, found: 621.2101.

4.3.7. N-(N′-(N″-Benzyl-N″-phenyl-3″-carboxamidophenyl)-N′-methyl-3′-carboxamidophenyl)-N-methyl-2-iodobenzamide ***8a′****.* Prepared according to general procedure C from amide **7a′** (82.0 mg, 0.123 mmol), NaH (60% solution in mineral oil) (7.00 mg, 0.175 mmol) and iodomethane (0.08 mL, 1.23 mmol). The crude mixture was purified through silica gel (3% MeOH/DCM) to afford an orange oil (m=77 mg, 92%). ^1H NMR ($CDCl_3$, 300 MHz) δ ppm 7.62 (d, J=7.6 Hz, 1H), 7.24–7.10 (m, 11H), 7.08–6.97 (m, 3H), 6.92–6.80 (m, 5H), 6.57 (d, J=7.3 Hz, 1H), 6.40 (d, J=6.9 Hz, 1H), 5.12 (s, 2H), 3.35 (s, 3H), 3.19 (s, 3H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ ppm 37.4, 38.3, 54.3, 93.7, 94.7, 127.3, 127.4, 127.7, 127.9, 128.2, 128.3, 128.6, 128.8, 129.0, 129.5, 130.2, 131.2, 131.8, 133.2, 136.5, 137.3, 137.3, 139.3, 141.8, 142.4, 143.4, 144.1. MS m/z (ESI^+) 702 (100%). HRMS calcd for $C_{36}H_{30}IN_3NaO_3$: 702.1230, found: 702.2056.

4.3.8. N-Benzyl-4-methyl-3-nitro-N-phenylbenzamide ***4b****.* Prepared according to general procedure A from the acid **2b** (1.83 g, 10.1 mmol), oxalyl chloride (2.17 mL, 25.2 mmol), amine (925 mg, 5.05 mmol) and Et_3N (0.84 mL, 5.05 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 6/4) to afford a white solid (1.91 g, 91%). IR (film) 1647, 1525 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 2.47 (s, 3H), 5.09 (s, 2H), 6.89 (m, 2H), 7.09 (d, J=7.9 Hz, 1H), 7.20–7.11 (m, 3H), 7.29–7.12 (m, 5H), 7.40 (dd, J=7.9, 1.8 Hz, 1H), 7.94 (d, J=1.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 20.4 (CH_3), 54.0 (CH_2), 125.3 (CH), 127.3 (CH), 127.5 (CH), 127.8 (CH), 128.5 (CH), 128.6 (CH), 129.4 (CH), 132.2 (CH), 132.9 (CH), 134.9 (Cq), 135.1 (Cq), 136.8 (Cq), 142.6 (Cq), 148.3 (Cq), 167.7 (Cq). HRMS calcd for $C_{21}H_{18}N_2Na\ O_3$: 369.1210, found: 369.1220. Mp=62–64 °C.

4.3.9. 1-N-Benzyl-4-methyl-3-N-(4-methyl-3-nitrobenzene)-1-N-phenylbenzene-1,3-diamide ***5b****.* Prepared according to general procedure B from nitroarene **4b** (1.71 g, 4.94 mmol), $SnCl_2\cdot 2H_2O$ (11.1 g, 49.4 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 6/4) to afford a white solid (1.53 g, 98%). IR (film) 3363, 1634 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 2.05 (s, 3H), 3.54 (br s, 2H), 5.11 (s, 2H), 6.54 (dd, J=7.7, 1.7 Hz, 1H), 6.76 (d, J=7.7 Hz, 1H), 6.80 (d, J=1.8 Hz, 1H), 6.93 (m, 2H), 7.18–7.06 (m, 3H), 7.32–7.21 (m, 5H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 17.2 (CH_3), 53.8 (CH_2), 115.5 (CH), 119.3 (CH), 124.1 (CH), 126.4 (CH), 127.2 (CH), 127.4 (CH), 128.2 (CH), 128.4 (CH), 128.8 (CH), 129.4 (CH), 134.5 (Cq), 137.7 (Cq), 144.8 (Cq), 144.0 (Cq), 144.1 (Cq), 170.6 (Cq). MS (ESI^+) m/z: 317 (62) [M+H], 339 (52) [M+Na]. HRMS calcd for $C_{21}H_{21}N_2O$: 317.1648, found: 317.1647. Mp=104–105 °C.

The amine was used to make the title compound by general procedure A using the acid (114 mg, 0.629 mmol), oxalyl chloride (0.27 mL, 3.16 mmol), amine (100 mg, 0.316 mmol) and pyridine (0.08 mL, 0.948 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 7/3) to afford a white solid (142 mg, 91%). IR (film) 3278, 1622 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz, High concentration) δ 2.17 (s, 3H), 2.70 (s, 3H), 5.12 (s, 2H), 6.83 (m, 2H), 6.98 (m,

2H), 7.22–7.09 (m, 3H), 7.31–7.24 (m, 5H), 7.44 (d, J=8.1 Hz, 1H), 7.52 (s, 1H), 8.16 (dd, J=7.9, 1.7H, 1H), 8.63 (d, J=1.7 Hz, 1H), 9.02 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 17.8 (CH_3), 20.5 (CH_3), 53.9 (CH_2), 123.8 (CH), 125.3 (CH), 125.8 (CH), 126.9 (CH), 127.4 (CH), 127.7 (CH), 128.3 (CH), 128.4 (CH), 129.1 (CH), 129.7 (CH), 131.9 (CH), 133.0 (CH), 133.7 (Cq), 133.7 (Cq), 133.8 (Cq), 135.2 (Cq), 136.9 (Cq), 137.0 (Cq), 142.7 (Cq), 149.0 (Cq), 163.6 (Cq), 170.7 (Cq). MS (ESI$^+$) m/z: 502 (100) [M+Na]. HRMS calcd for $C_{29}H_{25}N_3NaO_4$: 502.1737, found: 502.1744. Mp=126–130 °C.

4.3.10. 1-N-Benzyl-3-N,4-dimethyl-3-N-(4-methyl-3-nitrobenzene)-1-N-phenylbenzene-1,3-diamido ***6b***. Prepared according to general procedure C from amide **5b** (765 mg, 1.60 mmol), NaH (319 mg, 7.98 mmol), methyl iodide (0.5 mL, 7.98 mmol). The crude mixture was purified through silica gel (PE then PE/EtOAc: 7/3) to afford a white solid (733 mg, 93%). IR (film) 3061–2931, 1644, 1528 cm^{-1}. Ratio: >95/5. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.04 (s, 3H), 2.52 (s, 3H), 3.17 (s, 3H), 5.08 (m, 2H), 6.83 (m, 2H), 6.97 (d, J=8.0 Hz, 1H), 7.07 (d, J=8.0 Hz, 1H), 7.09–7.15 (m, 4H), 7.16–7.19 (m, 2H), 7.23–7.32 (m, 5H), 7.92 (d, J=1.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 17.5 (CH_3), 20.4 (CH_3), 37.6 (CH_3), 54.0 (CH_2), 125.0 (CH), 126.8 (CH), 127.4 (CH), 127.6 (CH), 128.3 (CH), 128.4 (CH), 128.7 (CH), 128.9 (CH), 129.0 (CH), 131.1 (CH), 132.1 (CH), 132.4 (CH), 134.4 (Cq), 135.1 (Cq), 135.3 (Cq), 136.6 (Cq), 137.0 (Cq), 142.1 (Cq), 143.1 (Cq), 148.2 (Cq), 167.5 (Cq), 168.6 (Cq). MS (ESI$^+$) m/z: 516 [M+Na]. HRMS calcd for $C_{30}H_{27}N_3NaO_4$: 516.1899, found: 516.1887. Mp=65–66 °C.

4.3.11. 1-N-Benzyl-3-N,4-dimethyl-3-N-{4-methyl-3-[(4-methyl-3-nitrobenzene)amido]benzene}-1-N-phenylbenzene-1,3-diamido ***7b***. Prepared according to general procedure B from nitro **6b** (346 mg, 0.702 mmol), $SnCl_2\cdot 2H_2O$ (789 mg, 3.50 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 6/4) to afford a yellow foam (321 mg, 99%). Ratio: >95/5. IR (film) 3458, 3357, 3059–2926, 1641 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.00 (s, 6H), 3.11 (s, 3H), 3.58 (br s, 2H), 5.07 (m, 2H), 6.02 (d, J=7.6 Hz, 1H), 6.66 (d, J=7.8 Hz, 1H), 6.70 (s, 1H), 6.79 (m, 2H), 6.86. (d, J=7.8 Hz, 1H), 7.06 (d, J=8.0 Hz, 1H), 7.08–7.15 (m, 4H), 7.22–7.29 (m, 5H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 17.2 (CH_3), 17.7 (CH_3), 37.5 (CH_3), 53.9 (CH_2), 115.1 (CH), 118.6 (CH), 124.1 (Cq), 126.7 (CH), 127.4 (CH), 127.7 (CH), 127.8 (CH), 128.4 (CH), 128.5 (CH), 129.0 (CH), 129.2 (CH), 130.7 (CH), 134.2 (Cq), 134.6 (Cq), 136.7 (Cq), 137.2 (Cq), 143.2 (Cq), 143.3 (Cq), 144.0 (Cq), 169.3 (Cq), 170.6 (Cq). MS (ESI$^+$) m/z: 486 (40) [M+Na]. HRMS calcd for $C_{30}H_{29}N_3NaO_2$: 486.2152, found: 486.2152.

This amine was used to make the title compound according to general procedure A from acid (247.7 mg, 1.36 mmol), oxalyl chloride (0.59 mL, 6.82 mmol), amine (316 mg, 0.682 mL) and pyridine (0.28 mL, 3.41 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 8/2 to 5/5) to afford a white foam (373 mg, 87%). IR (film) 3281, 3061–2928, 1644, 1527 cm^{-1}. Ratio: 90/10. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.01 (s, 3H), 2.13 (s, 3H), 2.67 (s, 3H), 3.12 (s, 3H) 5.08 (m, 2H), 6.41 (d, J=7.8, 1H), 6.70 (d, J=7.9 Hz, 1H), 6.84–6.92 (m, 2H), 7.09 (d, J=8.4 Hz, 1H), 7.11–7.17 (m, 4H), 7.19 (s, 1H), 7.22–7.29 (m, 5H), 7.40 (s, 1H), 7.41 (d, J=8.4 Hz, 1H), 8.09 (d, J=7.9 Hz, 1H), 8.58 (s, 1H), 9.19 (br s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 17.5 (CH_3), 17.8 (CH_3), 20.4 (CH_3), 37.3 (CH_3), 54.8 (CH_2), 123.7 (CH), 124.8 (CH), 125.9 (CH), 126.8 (CH), 127.3 (CH), 127.8 (CH), 128.1 (CH), 128.3 (CH), 128.4 (CH), 128.8 (CH), 129.0 (CH), 129.3 (CH), 130.9 (CH), 132.1 (CH), 132.9 (CH), 133.3 (Cq), 133.6 (Cq), 134.1 (Cq), 134.6 (Cq), 135.2 (Cq), 136.8 (Cq), 136.9 (Cq), 137.1 (Cq), 142.1 (Cq), 143.2 (Cq), 148.9 (Cq), 163.6 (Cq), 169.2 (Cq), 170.5 (Cq). MS (ESI$^+$) m/z: 649 (100) [M+Na]. HRMS calcd for $C_{38}H_{34}N_4NaO_5$: 649.2421, found: 649.2416.

4.3.12. N-(N′-(N″-Benzyl-N″-phenyl-3″-carboxamidophenyl)-N′-methyl-3′-carboxamidophenyl)-N-methyl-3-nitrobenzamide ***8b***. Prepared according to general procedure C from amide **7b** (276 mg, 0.441 mmol), NaH (88.0 mg, 2.20 mmol), methyl iodide (0.137 mL, 2.20 mmol). The crude mixture was purified through silica gel (PE to PE/EtOAc: 5/5) to afford a white foam (230 mg, 81%). ^{1}H NMR and ^{13}C NMR show mixture of multiple conformers resulting impossible to any ratio. MS (ESI$^+$) m/z: 663 (100) [M+Na]. HRMS calcd for $C_{39}H_{36}N_4NaO_5$: 663.2578, found: 663.2571.

4.3.13. 1-N,3-N-Dibenzyl-4-methyl-3-N-(4-methyl-3-nitrobenzene)-1-N-phenylbenzene-1,3-diamido ***6b′***. Prepared according to general procedure C from amide **5b** (103 mg, 0.209 mmol), NaH (33.0 mg, 0.835 mmol), benzyl bromide (0.25 mL, 2.09 mmol). The crude mixture was purified through silica gel (PE then PE/EtOAc: 7/3) to afford a white solid (110 mg, 92%). IR (film) 3064, 1648, 1528 cm^{-1}. Ratio: >95/5. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.50 (s, 3H), 2.50 (s, 3H), 4.55 (d, J=13.7 Hz, 1H), 5.01 (d, J=13.7 Hz, 1H), 5.07 (d, J=14.5 Hz, 1H), 5.11 (d, J=14.5 Hz, 1H), 6.82 (d, J=7.9 Hz, 1H), 6.87–6.92 (m, 2H), 7.01 (d, J=7.9 Hz, 1H), 7.05–7.32 (m, 16H), 7.99 (m, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 17.3 (CH_3), 20.3 (CH_3), 53.9 (CH_2), 54.0 (CH_2), 125.2 (CH), 127.0 (CH), 127.4 (CH), 127.8 (CH), 127.9 (CH), 128.3 (CH), 128.4 (CH), 128.4 (CH), 128.7 (CH), 129.1 (CH), 129.3 (CH), 129.4 (CH), 131.0 (CH), 131.9 (CH), 132.4 (CH), 134.6 (Cq), 134.9 (Cq), 135.2 (Cq), 135.7 (Cq), 137.0 (Cq), 137.7 (Cq), 140.1 (Cq), 143.3 (Cq), 148.3 (Cq), 167.0 (Cq), 168.7 (Cq). MS (ESI$^+$) m/z: 592 (100) [M+Na]. HRMS calcd for $C_{36}H_{31}N_3NaO_4$: 592.2207, found: 592.2217. Mp=56–58 °C.

4.3.14. 1-N,3-N-Dibenzyl-4-methyl-3-N-{4-methyl-3-[(4-methyl-3-nitrobenzene)amido]benzene}-1-N-phenylbenzene-1,3-diamido ***7b′***. Prepared according to general procedure B from nitro **6b′** (580 mg, 1.02 mmol), $SnCl_2\cdot 2H_2O$ (2.30 g, 10.2 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 6/4) to afford a yellow solid (512 mg, 93%). IR (film) 3454–3359, 1637, 1590 cm^{-1}. Ratio: >95/5. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.48 (s, 3H), 2.02 (s, 3H), 3.50 (br s, 2H), 4.50 (d, J=13.9 Hz, 1H), 4.94 (d, J=13.9 Hz, 1H), 5.05 (d, J=14.5 Hz, 1H), 5.11 (d, J=14.5 Hz, 1H), 6.18 (dd, J=7.7, 1.4 Hz, 1H), 6.64 (d, J=7.8 Hz, 1H), 6.72 (d, J=1.5 Hz, 1H), 6.76 (d, J=7.8 Hz, 1H), 6.84–6.89 (m, 2H), 7.04–7.33 (m, 15H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 17.2 (CH_3), 17.6 (CH_3), 53.8 (CH_2), 53.9 (CH_2), 115.4 (CH), 119.0 (CH), 124.3 (Cq), 126.9 (CH), 127.3 (CH), 127.4 (CH), 127.8 (CH), 127.9 (CH), 128.2 (CH), 128.3 (CH), 128.4 (CH), 129.1 (CH), 129.2 (CH) 129.3 (CH), 130.7 (CH), 134.2 (Cq), 134.4 (Cq), 136.6 (Cq), 137.2 (Cq), 138.1 (Cq), 141.2 (Cq), 143.4 (Cq), 143.8 (Cq), 169.3 (Cq), 169.8 (Cq). MS (ESI$^+$) m/z: 562 (100) [M+Na]. HRMS calcd for $C_{36}H_{34}N_3O_2$: 540.2651, found: 540.2640.

The amine was used to make the title compound by general procedure A from the acid (134 mg, 0.740 mmol), oxalyl chloride (0.32 mL, 3.71 mmol), amine (200 mg, 0.371 mL) and pyridine (0.09 mL, 1.11 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 6/4) to afford a white solid (202 mg, 77%). IR (film) 3435, 1641, 1526 cm^{-1}. Ratio: >95/5. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.48 (s, 3H), 2.12 (s, 3H), 2.67 (s, 3H), 4.41 (d, J=13.8 Hz, 1H), 5.03 (d, J=13.8 Hz, 1H), 5.07 (d, J=14.5 Hz, 1H), 5.11 (d, J=14.5 Hz, 1H), 6.39 (dd, J=7.9, 1.6 Hz, 1H), 6.67 (d, J=8.1 Hz, 1H), 6.74 (d, J=8.1 Hz, 1H), 6.92 (m, 2H), 7.02 (m, 2H), 7.13 (m, 3H), 7.16–7.23 (m, 6H), 7.25–7.31 (m, 4H), 7.42 (m, 2H), 8.11 (dd, J=8.0, 1.6 Hz, 1H), 8.57 (d, J=1.6 Hz, 1H), 9.01 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 17.7 (CH_3), 18.1 (CH_3), 20.8 (CH_3), 54.0 (CH_2), 54.3 (CH_2), 123.7 (CH), 125.1 (CH), 126.5 (CH), 126.9 (CH), 127.4 (CH), 127.7 (CH), 128.0 (CH), 128.1 (CH), 128.3 (CH), 128.4 (CH), 129.1 (CH), 129.2 (CH), 129.3 (CH), 129.4 (CH), 131.0 (CH), 132.0 (CH), 133.0 (CH), 133.4 (Cq), 133.6 (Cq), 134.1 (Cq), 134.4 (Cq), 135.0 (Cq), 136.0 (Cq), 136.9 (Cq), 137.1 (Cq), 138.3 (Cq), 140.2 (Cq), 143.4 (Cq), 149.0 (Cq), 163.7 (Cq), 169.4 (Cq), 170.0 (Cq). MS (ESI$^+$) m/z: 725 (100) [M+Na]. HRMS calcd for $C_{44}H_{38}N_4NaO_5$: 725.2740, found: 725.2744. Mp=118–124 °C.

4.3.15. 1-N,3-N-Dibenzyl-3-N-{3-[benzyl(4-methyl-3-nitrobenzene)amido]-4-methylbenzene}-4-methyl-1-N-phenylbenzene-1,3-

diamido ***8b***′. Prepared according to general procedure C from amide **7b**′ (50.0 mg, 0.071 mmol), NaH (12.0 mg, 0.284 mmol), benzyl bromide (0.085 mL, 0.716 mmol). The crude mixture was purified through silica gel (PE to PE/EtOAc: 7/3) to afford a colourless oil (55 mg, 98%). ^{1}H NMR and ^{13}C NMR show mixture of multiple conformers resulting impossible to any ratio. MS (ESI$^+$) *m*/*z*: 815 (100) [M+Na]. HRMS calcd for $C_{51}H_{44}N_4NaO_5$: 815.3204, found: 815.3193.

4.3.16. N,2-Dimethyl-3-nitro-N-phenylbenzamide ***4c***. Prepared according to general procedure A from acid (2.00 g, 11.0 mmol), oxalyl chloride (4.72 mL, 55.8 mmol), *N*-methylaniline (2.38 mL, 22.0 mmol) and Et_3N (3.06 mL, 21.9 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 8/2) to afford a colourless solid (*m*=3.1 g, 99%). IR (film) 3064–2937, 1649, 1528 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.50 (s, 3H), 3.53 (s, 3H), 6.60 (m, 2H), 7.29–7.09 (m, 5H), 7.69 (d, *J*=7.9 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 16.8 (CH_3), 37.3 (CH_3), 124.5 (CH), 126.1 (CH), 126.6 (CH), 127.5 (CH), 129.3 (CH), 129.9 (Cq), 131.6 (CH), 139.9 (Cq), 142.9 (Cq), 150.0 (Cq), 168.8 (Cq). MS (EI) *m*/*z*: 271 (100) [M+H]. HRMS calcd for $C_{15}H_{15}N_2O_3$: 271.1077, found: 271.1077. Mp=78–79 °C.

4.3.17. N-Benzyl-2-methyl-3-nitro-N-phenylbenzamide ***4c***′. Prepared according to general procedure A from acid (2.00 g, 11.0 mmol), oxalyl chloride (4.72 mL, 55.8 mmol), *N*-benzylaniline (4.08 mL, 23.6 mmol) and Et_3N (3.06 mL, 21.9 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 9/1 then 8/2) to afford a white solid (*m*=3.72 g, 98%). IR (film) 1649, 1527 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.52 (s, 3H), 5.12 (s, 2H), 6.85–6.79 (m, 2H), 7.15–7.05 (m, 4H), 7.32–7.22 (m, 6H), 7.67 (d, *J*=8.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 16.8 (CH_3), 53.1 (CH_2), 124.4 (CH), 126.0 (CH), 127.8 (CH), 127.9 (CH), 128.6 (CH), 128.9 (CH), 129.2 (CH), 129.9 (Cq), 131.5 (CH), 136.8 (Cq), 139.7 (Cq), 141.3 (Cq), 150.0 (Cq), 168.7 (Cq). MS (EI) *m*/*z*: 347 (51) [M+H]. HRMS calcd for $C_{21}H_{19}N_2O_3$: 347.1390, found: 347.1398. Mp=104–105 °C.

4.3.18. 1-N,2-Dimethyl-3-N-(2-methyl-3-nitrobenzene)-1-N-phenylbenzene-1,3-dicarboxamide ***5c***. Prepared according to general procedure B from nitro **4c** (100 mg, 0.370 mmol), $SnCl_2\cdot 2H_2O$ (652 mg, 2.89 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 6/4) to afford a colourless oil (*m*=81 mg, 91%). IR (film) 3357, 3059–2929, 1636, 1589 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.09 (br s, 3H), 3.50 (br s, 3H), 3.61 (br s, 2H), 6.49 (br m, 2H), 6.79 (br t, *J*=7.0 Hz, 1H), 6.94–7.21 (br m, 5H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.2 (CH_3), 37.1 (CH_3), 115.1 (CH), 117.9 (CH), 118.8 (Cq), 125.9 (CH), 126.4 (CH), 126.5 (CH), 128.7 (CH), 137.6 (Cq), 143.8 (Cq), 144.4 (Cq), 171.4 (Cq). MS (EI) *m*/*z*: 241 (100) [M+H]. HRMS calcd for $C_{15}H_{17}N_2O$: 241.1335, found: 241.1331.

This amine was used to make the title compound according to general procedure A from acid (307 mg, 1.69 mmol), oxalyl chloride (0.73 mL, 8.63 mmol), amine (204 mg, 0.850 mmol) and Et_3N (0.24 mL, 1.72 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 6/4) to afford a white solid (*m*=201 mg, 82%). IR (film) 3243, 3055, 1645, 1528 cm^{-1}. Ratio 85/15: ^{1}H NMR ($CDCl_3$, 500 MHz) δ major conformer 2.19 (s, 3H), 2.60 (s, 3H), 3.44 (s, 3H), 6.84 (d, *J*=7.4 Hz, 1H), 6.98 (m, 3H), 7.11 (m, 1H), 7.19 (t, *J*=7.4 Hz, 2H), 7.42 (t, *J*=7.7 Hz, 1H), 7.66 (m, 2H), 7.71 (br s, 1H), 7.90 (d, *J*=8.0 Hz, 1H). Minor conformer 1.61 (br s, 3H), 2.65 (s, 3H), 3.17 (s, 3H), other signals masked by major conformer. ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.9 (CH_3), 16.1 (CH_3), 37.2 (CH_3), 124.6 (CH), 124.9 (CH), 125.3 (CH), 125.8 (CH), 126.4 (CH), 126.7 (CH), 127.1 (CH), 127.8 (Cq), 129.2 (CH), 130.5 (Cq), 130.8 (CH), 135.6 (Cq), 137.5 (Cq), 139.9 (Cq), 143.2 (Cq), 150.8 (Cq), 166.4 (Cq), 170.6 (Cq). MS (ESI$^+$) *m*/*z*: 426 (90) [M+Na]. HRMS calcd for $C_{23}H_{21}N_3NaO_4$: 426.1424, found: 426.1417. Mp=89–94 °C.

4.3.19. 1-N-Benzyl-2-methyl-3-N-(2-methyl-3-nitrobenzene)-1-N-phenylbenzene-1,3-dicarboxamide ***5c***′. Prepared according to general procedure B from nitro **4c**′ (200 mg, 0.578 mmol), $SnCl_2\cdot 2H_2O$ (1.30 g, 5.78 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 6/4) to afford a colourless oil (*m*=177 mg, 97%). IR (film) 3360, 3062–2857, 1643, 1591 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.14 (s, 3H), 3.71 (br s, 2H), 5.13 (br s, 2H), 6.50 (m, 2H), 6.77 (m, 1H), 6.84 (m, 2H), 6.98–7.12 (m, 3H), 7.20–7.34 (m, 5H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.0 (CH_3), 52.4 (CH_2), 114.7 (CH), 117.2 (CH), 118.4 (Cq), 125.5 (CH), 126.5 (CH), 127.0 (CH), 127.3 (CH), 128.1 (CH), 128.2 (CH), 128.3 (CH), 137.0 (Cq), 137.3 (Cq), 141.9 (Cq), 144.7 (Cq), 171.1 (Cq). MS (EI) *m*/*z*: 317 (100) [M+H]. HRMS calcd for $C_{21}H_{20}N_2O$: 317.1648, found: 317.1646.

This amine was used to make the title compound according to general procedure A from acid (203 mg, 1.12 mmol), oxalyl chloride (0.48 mL, 5.67 mmol), amine (177 mg, 0.560 mmol) and pyridine (0.14 mL, 1.68 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 6/4) to afford a white solid (*m*=250 mg, 93%). IR (film) 3433, 1643, 1526 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.12 (s, 3H), 2.57 (s, 3H), 4.98 (s, 2H), 6.79 (m, 3H), 6.94 (t, *J*=7.8 Hz, 1H), 7.03–7.13 (m, 3H), 7.16–7.23 (m, 2H), 7.24–7.30 (m, 3H), 7.35 (t, *J*=7.9 Hz, 1H), 7.47 (d, *J*=7.9 Hz, 1H), 7.65 (d, *J*=7.5 Hz, 1H), 7.85 (d, *J*=8.0 Hz, 1H), 8.30 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.9 (CH_3), 16.1 (CH_3), 52.9 (CH_2), 124.7 (CH), 124.8 (CH), 125.3 (CH), 125.8 (CH), 126.7 (CH), 127.4 (CH), 127.5 (CH), 127.6 (CH), 127.9 (Cq), 128.4 (CH), 128.5 (CH), 129.0 (CH), 130.6 (Cq), 130.8 (CH), 135.6 (Cq), 136.9 (Cq), 137.4 (Cq), 139.8 (Cq), 141.5 (Cq), 150.8 (Cq), 166.4 (Cq), 170.5 (Cq). MS (ESI$^+$) *m*/*z*: 497 (40) [M+NH$_4$], 502 (100) [M+Na]. HRMS calcd for $C_{29}H_{29}N_4O_4$: 497.2183, found: 497.2195. Mp=185–190 °C.

4.3.20. 1-N-Benzyl-2-methyl-3-N-(2-nitrobenzene)-1-N-phenylbenzene-1,3-dicarboxamide ***5d***. Prepared according to general procedure A from acid (210 mg, 1.26 mmol), oxalyl chloride (0.54 mL, 6.33 mmol), amine derived from **4c**′ (200 mg, 0.633 mmol) and pyridine (0.15 mL, 1.85 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 6/4 then EtOAc) to afford a white solid (275 mg, 95%). IR (film) 3436, 1640, 1527 cm^{-1}. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 2.27 (s, 3H), 5.14 (s, 2H), 7.18–7.00 (m, 7H), 7.37–7.23 (m, 6H), 7.92–7.70 (m, 3H), 8.14 (d, *J*=7.9 Hz, 1H), 10.1 (br s, 1H). ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ 14.9 (CH_3), 51.9 (CH_2), 124.2 (CH), 125.0 (CH), 125.2 (CH), 125.9 (CH), 127.0 (CH), 127.2 (CH), 127.7 (CH), 127.9 (CH), 128.4 (CH), 128.8 (CH), 129.3 (CH), 129.6 (Cq), 130.8 (CH), 132.7 (Cq), 134.0 (CH), 135.8 (Cq), 137.4 (Cq), 137.9 (Cq), 141.7 (Cq), 146.5 (Cq), 164.4 (Cq), 169.5 (Cq). MS (ESI$^+$) *m*/*z*: 466 (100) [M+H]. HRMS calcd for $C_{28}H_{24}N_3O_4$: 466.1761, found: 466.1757.

4.3.21. 1-N-Benzyl-2-methyl-3-N-(4-nitrobenzene)-1-N-phenylbenzene-1,3-dicarboxamide ***5e***. Prepared according to general procedure A from acid chloride (265 mg, 1.43 mmol), amine derived from **4c**′ (226 mg, 0.715 mmol) and pyridine (0.17 mL, 2.14 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 6/4) to afford a white solid (284 mg, 86%). IR (film) 3437, 1639, 1527 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.12 (s, 3H), 5.11 (s, 2H), 6.89–6.81 (m, 2H), 6.94 (t, *J*=7.8 Hz, 1H), 7.13–7.04 (m, 3H), 7.18 (br s, 1H), 7.29 (m, 4H), 7.41 (br s, 1H), 8.09 (br s, 1H), 8.30–8.19 (m, 3H), 8.38 (m, 1H), 8.70 (br s, 1H). ^{13}C NMR (DMSO-d_6, 125 MHz) δ 15.1 (CH_3), 51.9 (CH_2), 123.6 (CH), 123.7 (CH), 125.2 (CH), 125.4 (CH), 126.8 (CH), 126.9 (CH), 127.2 (CH), 127.7 (CH), 127.9 (CH), 128.4 (CH), 128.8 (CH), 129.2 (CH), 130.7 (CH), 136.1 (Cq), 137.4 (Cq), 137.8 (Cq), 139.9 (Cq), 141.7 (Cq), 149.2 (Cq), 150.0 (Cq), 163.7 (Cq), 169.5 (Cq). MS (ESI$^+$) *m*/*z*: 483 (90) [M+NH$_4$], 488 (100) [M+Na]. HRMS calcd for $C_{28}H_{27}N_4O_4$: 483.2027, found: 483.2022. Mp=224–226 °C.

4.3.22. 1-N,2,3-N-Trimethyl-1-N-(2-methyl-3-nitrobenzene)-3-N-phenylbenzene-1,3-dicarboxamide ***6c***. Prepared according to general procedure C from amide **5c** (81.0 mg, 0.201 mmol), NaH (32.0 mg, 0.800 mmol) and MeI (0.13 mL, 2.09 mmol). The crude mixture was purified through silica gel (PE then PE/EtOAc 9/1, 6/4,

4/6) to afford a white solid (m=66 mg, 79%). IR (film) 2932, 1647, 1528 cm^{-1}. Ratio: 80/20. ^1H NMR ($CDCl_3$, 300 MHz) δ major conformer: 2.25 (s, 3H), 2.48 (s, 3H), 3.25 (s, 3H), 3.46 (s, 3H), 6.74–6.93 (m, 4H), 6.95–7.12 (m, 6H), 7.68 (dd, J=2.3, 6.9 Hz, 1H). Minor conformer: 2.32 (s, 3H), 2.59 (s, 3H), 2.97 (s, 3H), 3.53 (s, 3H), 7.13–7.23 (m, 4H), 7.33–7.57 (m, 4H), 7.92 (d, J=7.7 Hz, 1H), other signals masked by major conformer. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ major conformer: 15.2 (CH_3), 16.9 (CH_3), 36.8 (CH_3), 37.3 (CH_3), 124.5 (CH), 125.9 (CH), 126.3 (CH), 126.4 (CH), 126.9 (CH), 127.7 (CH), 128.4 (CH), 128.8 (CH), 130.2 (CH), 131.7 (Cq), 138.9 (Cq), 139.2 (Cq), 142.1 (Cq), 143.1 (Cq), 150.1 (Cq), 168.7 (Cq), 169.5 (Cq). MS (ESI^+) m/z: 440 (100) [M+Na]. HRMS calcd for $C_{24}H_{23}N_3NaO_4$: 440.1581, found: 440.1583. Mp=232–240 °C.

4.3.23. 1-N-Benzyl-2,3-N-dimethyl-3-N-(2-methyl-3-nitrobenzene)-1-N-phenylbenzene-1,3-dicarboxamide ***6c′***. Prepared according to general procedure C from amide **5c′** (75.0 mg, 0.156 mmol), NaH (25.0 mg, 0.625 mmol) and MeI (0.1 mL, 1.56 mmol). The crude mixture was purified through silica gel (PE then PE/EtOAc 9/1, 8/2, 6/4) to afford a pale yellow solid (m=57 mg, 74%). IR (film) 3062, 1646, 1528 cm^{-1}. Ratio: 80/20. ^1H NMR ($CDCl_3$, 300 MHz) δ major conformer: 2.30 (s, 3H), 2.49 (s, 3H), 3.26 (s, 3H), 5.05 (d, J=14.3 Hz, 1H), 5.09 (d, J=14.3 Hz, 1H), 6.68–6.77 (m, 2H), 6.80 (t, J=7.5 Hz, 1H), 6.90 (dd, J=7.5, 1.1 Hz, 1H), 6.96–7.07 (m, 6H), 7.26–7.35 (m, 5H), 7.66 (dd, J=6.9, 2.6 Hz, 1H). Minor conformer: 2.35 (s, 3H), 2.59 (s, 3H), 2.96 (s, 3H), 5.26 (d, J=14.5, 1H), 7.92 (d, J=8.1 Hz, 1H), other signals masked by major conformer. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ major conformer: 15.3 (CH_3), 16.9 (CH_3), 36.8 (CH_3), 53.0 (CH_2), 124.4 (CH), 125.9 (CH), 126.3 (CH), 127.3 (CH), 127.5 (CH), 127.6 (CH), 127.6 (CH), 128.3 (CH), 128.4 (CH), 128.6 (CH), 128.8 (CH), 130.2 (CH), 130.3 (Cq), 131.7 (Cq), 137.0 (Cq), 138.8 (Cq), 139.2 (Cq), 141.6 (Cq), 142.2 (Cq), 150.1 (Cq), 168.8 (Cq), 169.4 (Cq). MS (ESI^+) m/z: 511 (62) [M+NH_4], 516 (100) [M+Na]. HRMS calcd for $C_{30}H_{31}N_4O_4$: 511.2340, found: 511.2347. Mp=156–157 °C.

4.3.24. 1-N,3-N-Dibenzyl-2-methyl-1-N-(2-methyl-3-nitrobenzene)-3-N-phenylbenzene-1,3-dicarboxamide ***6c′***. Prepared according to general procedure C from amide **5c′** (60.0 mg, 0.125 mmol), NaH (20.0 mg, 0.500 mmol), benzyl bromide (0.15 mL, 1.25 mmol). The crude mixture was purified through silica gel (PE then PE/EtOAc: 7/3) to afford a colourless oil (m=71 mg, 100%). IR (film) 3064, 1648, 1528 cm^{-1}. Ratio 85/15. ^1H NMR ($CDCl_3$, 300 MHz) δ major conformer: 2.28 (s, 3H), 2.42 (s, 3H), 3.98 (d, J=13.5 Hz, 1H), 5.07 (br s, 2H), 5.66 (d, J=13.5 Hz, 1H), 6.23 (d, J=7.9 Hz, 1H), 6.62 (t, J=7.9 Hz, 1H), 6.73 (m, 2H), 6.87 (d, J=7.5 Hz, 1H), 7.36–6.93 (m, 15H), 7.64 (dd, J=7.5, 1.4 Hz, 1H). Minor conformer: 2.22 (s, 3H), 2.36 (s, 3H), 7.96 (d, J=7.8 Hz, 1H), other signals masked by major conformer. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ major conformer: 15.2 (CH_3), 16.7 (CH_3), 52.0 (CH_2), 53.0 (CH_2), 124.5 (CH), 125.7 (CH), 126.0 (CH), 127.3 (CH), 127.6 (CH), 127.6 (CH), 127.9 (CH), 128.4 (CH), 128.5 (CH), 128.7 (CH), 128.8 (CH), 129.5 (CH), 129.8 (CH), 129.9 (CH), 130.2 (Cq), 131.9 (Cq), 136.2 (Cq), 137.1 (Cq), 138.7 (Cq), 139.1 (Cq), 139.9 (Cq), 141.7 (Cq), 150.1 (Cq), 168.5 (Cq), 169.5 (Cq). MS (ESI^+) m/z: 592 (100) [M+Na]. HRMS calcd for $C_{36}H_{31}N_3NaO_4$: 592.2207, found: 592.2201. Mp=60–62 °C.

4.3.25. 1-N-Benzyl-2,3-N-dimethyl-3-N-(2-nitrobenzene)-1-N-phenylbenzene-1,3-dicarboxamide ***6d***. Prepared according to general procedure C from amide **5d** (200 mg, 0.430 mmol), NaH (69.0 mg, 1.72 mmol), methyl iodide (0.27 mL, 4.34 mmol). The crude mixture was purified through silica gel (PE then PE/EtOAc: 6/4) to afford a yellow solid (177 mg, 86%). IR (film) 3060, 1644, 1526 cm^{-1}. Ratio: 84/16. ^1H NMR (DMSO-d_6, 300 MHz) major conformer δ 2.33 (s, 3H), 3.26 (s, 3H), 5.04 (d, J=14.2 Hz, 1H), 5.13 (d, J=14.2 Hz, 1H), 6.77–6.69 (m, 2H), 6.86 (d, J=7.3 Hz, 1H), 6.97 (d, J=7.8 Hz, 1H), 7.04–7.00 (m, 2H), 7.07 (dd, J=7.3, 1.4 Hz, 1H), 7.43–7.19 (m, 9H), 7.90 (dd, J=7.8, 1.1 Hz, 1H). Minor conformer δ 2.41 (s, 3H), 2.97 (s, 3H), 5.27 (d, J=14.5 Hz, 1H), 7.52 (d, J=7.7 Hz, 1H), 7.71 (t, J=7.7 Hz, 1H), 7.77 (t, J=7.4 Hz, 1H), 8.25 (d, J=8.2 Hz, 1H), other signals masked by major conformer. ^{13}C NMR ($CDCl_3$, 75.5 MHz) major conformer δ 15.2 (CH_3), 36.6 (CH_3), 52.9 (CH_2), 124.4 (CH), 126.3 (CH), 127.1 (CH), 127.4 (CH), 127.5 (CH), 127.5 (CH), 127.6 (CH), 128.1 (CH), 128.5 (CH), 128.6 (CH), 128.7 (CH), 129.4 (CH), 131.9 (Cq), 132.8 (Cq), 133.3 (CH), 137.0 (Cq), 138.5 (Cq), 141.6 (Cq), 142.0 (Cq), 145.6 (Cq), 167.2 (Cq), 169.5 (Cq). Minor conformer δ 39.0 (CH_3), 52.3 (CH_2), 126.6 (CH), 127.2 (CH), 128.0 (CH), 128.4 (CH), 128.8 (CH), 129.9 (CH), 134.7 (CH), other signals masked by major conformer. MS (ESI^+) m/z: 502 (100) [M+Na]. HRMS calcd for $C_{29}H_{25}N_3NaO_4$: 502.1737, found: 502.1745. Mp=98–100 °C.

4.3.26. 1-N-Benzyl-2,3-N-dimethyl-3-N-(4-nitrobenzene)-1-N-phenylbenzene-1,3-dicarboxamide ***6e***. Prepared according to general procedure C from amide **5e** (100 mg, 0.215 mmol), NaH (34.4 mg, 0.860 mmol), methyliodide (0.13 mL, 2.15 mmol). The crude mixture was purified through silica gel (PE then PE/EtOAc: 6/4) to afford a white solid (80 mg, 78%). IR (film) 3061, 1646, 1527 cm^{-1}. Ratio: 95/5. ^1H NMR ($CDCl_3$, 300 MHz) δ 2.29 (s, 3H), 3.30 (s, 3H), 5.07 (d, J=14.2 Hz, 1H), 5.12 (d, J=14.2 Hz, 1H), 6.79 (m, 3H), 6.92 (t, J=7.7 Hz, 1H), 7.06 (m, 3H), 7.14 (m, 1H), 7.24 (d, J=8.8 Hz, 2H), 7.31 (m, 5H), 7.91 (d, J=8.8 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 15.0 (CH_3), 37.4 (CH_3), 53.1 (CH_2), 122.8 (CH), 126.5 (CH), 127.4 (CH), 127.5 (CH), 127.6 (CH), 127.9 (CH), 128.5 (CH), 128.7 (CH), 128.8 (CH), 128.9 (CH), 129.0 (CH), 131.5 (Cq), 136.9 (Cq), 139.2 (Cq), 141.4 (Cq), 141.5 (Cq), 142.8 (Cq), 147.8 (Cq), 168.3 (Cq), 169.4 (Cq). MS (ESI^+) m/z: 497 (38) [M+NH_4], 502 (100) [M+Na]. HRMS calcd for $C_{29}H_{29}N_4O_4$: 497.2183, found: 497.2179. Mp=100–102 °C.

4.3.27. 1-N,2,3-N-Trimethyl-1-N-{2-methyl-3-[(2-methyl-3-nitrobenzene)amido]benzene}-3-N-phenylbenzene-1,3-dicarboxamide ***7c***. Prepared according to general procedure B from nitro **6c** (129 mg, 0.309 mmol), $SnCl_2 \cdot 2H_2O$ (349 mg, 1.55 mmol). The crude mixture was purified through silica gel (toluene/EtOAc: 4/6) to afford a white solid (m=100 mg, 84%). IR (film) 3370, 1645, 1528 cm^{-1}. Ratio 78/22. ^1H NMR ($CDCl_3$, 500 MHz) δ major conformer: 2.12 (s, 3H), 2.29 (s, 3H), 3.23 (s, 3H), 3.47 (s, 3H), 3.61 (br s, 2H), 6.28 (d, J=7.4 Hz, 1H), 6.48 (d, J=7.7 Hz, 1H), 6.69 (t, J=7.7 Hz, 1H), 6.73–6.82 (m, 4H), 6.99–7.11 (m, 3H), 7.16 (m, 1H). Minor conformer 2.19 (s, 3H), 2.33 (s, 3H), 2.95 (s, 3H), 3.53 (s, 3H), other signals masked by major conformer. ^{13}C NMR ($CDCl_3$, 125 MHz) δ major conformer: 14.4 (CH_3), 15.2 (CH_3), 36.5 (CH_3), 37.0 (CH_3), 115.2 (CH), 116.5 (CH), 119.0 (Cq), 125.9 (CH), 126.2 (CH), 126.6 (CH), 126.9 (CH), 127.1 (CH), 128.6 (CH), 128.9 (CH), 131.9 (Cq), 137.0 (Cq), 138.1 (Cq), 143.2 (Cq), 144.9 (Cq), 145.1 (Cq), 169.8 (Cq), 171.4 (Cq). MS (ESI^+) m/z: 388 (100) [M+H]. HRMS calcd for $C_{24}H_{26}N_3O_2$: 388.2020, found: 388.2030. Mp=241–242 °C.

This amine was used to make the title compound according to general procedure A from acid (49.0 mg, 0.268 mmol), oxalyl chloride (0.11 mL, 1.34 mmol), amine (52.0 mg, 0.134 mmol) and Et_3N (0.037 mL, 0.268 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 1/9) to afford a colourless oil (65 mg, 88%). IR (film) 3249, 3056, 1627 cm^{-1}. Ratio: 77/23. ^1H NMR ($CDCl_3$, 300 MHz) δ major conformer: 2.16 (s, 3H), 2.21 (s, 3H), 2.55 (s, 3H), 3.10 (s, 3H), 3.43 (s, 3H), 6.51 (d, J=7.2 Hz, 1H), 6.69–7.18 (m, 9H), 7.37 (t, J=7.8 Hz, 1H), 7.51–7.70 (m, 2H), 7.86 (d, J=7.8 Hz, 1H), 8.20 (br s, 1H). Minor conformer: 2.17 (s, 3H), 2.59 (s, 3H), 2.88 (s, 3H) 3.50 (s, 3H), 8.72 (br s, 1H), other signals masked by major conformer. ^{13}C NMR ($CDCl_3$, 125 MHz) δ major conformer: 15.1 (CH_3), 15.1 (CH_3), 16.1 (CH_3), 36.7 (CH_3), 37.2 (CH_3), 123.6 (CH), 124.6 (CH), 125.3 (CH), 125.6 (CH), 126.2 (CH), 126.7 (CH), 126.8 (CH), 127.3 (CH), 128.4 (CH), 129.0 (CH), 130.4 (Cq), 130.7 (CH), 130.9 (CH), 131.7 (Cq), 136.0 (Cq), 136.9 (Cq), 138.6 (Cq), 139.6 (Cq), 139.8 (Cq), 142.6 (Cq), 143.1 (Cq), 150.8 (Cq), 166.3 (Cq), 169.7 (Cq), 170.5 (Cq). MS

(ESI$^+$) *m/z*: 551 (80) [M+H], 573 (57) [M+Na]. HRMS calcd for $C_{32}H_{31}N_4O_5$: 551.2289, found: 551.2292. Mp=156–158 °C.

4.3.28. 1-N-Benzyl-2,3-N-dimethyl-3-N-{2-methyl-3-[(2-methyl-3-nitrobenzene)amido]benzene}-1-N-phenylbenzene-1,3-dicarboxamide ***7c′***. Prepared according to general procedure B from nitro **6c′** (514 mg, 1.04 mmol), $SnCl_2\cdot 2H_2O$ (2.34 g, 10.4 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 2/8) to afford a white solid (460 mg, 96%). IR (film) 3455–3360, 1640, 1592 cm^{-1}. Ratio: 75/25. ^{1}H NMR ($CDCl_3$, 300 MHz) δ major conformer: 2.17 (s, 3H), 2.32 (s, 3H), 3.22 (s, 3H), 5.05 (d, *J*=14.2 Hz, 1H), 5.14 (d, *J*=14.6 Hz, 1H), 6.31 (d, *J*=7.2 Hz, 1H), 6.57 (d, *J*=7.7 Hz, 1H), 6.75–6.67 (m, 3H), 6.80 (m, 1H), 6.86 (m, 1H), 7.02 (m, 3H), 7.11 (m, 1H), 7.35–7.26 (m, 5H). Minor conformer: 2.23 (s, 3H), 2.35 (s, 3H), 2.95 (s, 3H), 5.26 (d, *J*=14.1 Hz, 1H), other signals masked by major conformer. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ major conformer: 14.4 (CH_3), 15.2 (CH_3), 36.4 (CH_3), 52.6 (CH_2), 115.1 (CH), 116.1 (CH), 118.9 (Cq), 125.6 (CH), 126.8 (CH), 127.1 (CH), 127.3 (CH), 127.4 (CH), 128.3 (CH), 128.3 (CH), 128.4 (CH), 128.6 (CH), 128.7 (CH), 131.7 (Cq), 136.8 (Cq), 137.1 (Cq), 137.9 (Cq), 141.6 (Cq), 143.0 (Cq), 144.7 (Cq), 169.6 (Cq), 171.4 (Cq). MS (ESI$^+$) *m/z*: 464 (100) [M+H], 481 (78) [M+NH_4]. HRMS calcd for $C_{30}H_{30}N_3O_2$: 464.2333, found: 464.2342. Mp=70–71 °C.

This amine was used to make the title compound according to general procedure A from acid (78.0 mg, 0.432 mmol), oxalyl chloride (0.19 mL, 2.16 mmol), amine (100 mg, 0.216 mmol) and Et_3N (0.06 mL, 0.432 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 3/7) to afford a white solid (127 mg, 94%). IR (film) 3253, 3061, 1630 cm^{-1}. Ratio: 75/25. ^{1}H NMR ($CDCl_3$, 300 MHz) δ major conformer: 2.20 (s, 3H), 2.29 (s, 3H), 2.57 (s, 3H), 3.16 (s, 3H), 5.05 (d, *J*=14.4 Hz, 1H), 5.08 (d, *J*=14.4 Hz, 1H), 6.55 (d, *J*=7.2 Hz, 1H), 6.66–6.89 (m, 5H), 6.94–7.12 (m 4H), 7.28 (m, 4H), 7.40 (t, *J*=8.1 Hz, 1H), 7.62–772 (m, 2H), 7.77 (br s, 1H), 7.89 (d, *J*=7.8 Hz, 1H). Minor conformer 2.16 (s, 3H), 2.24 (s, 3H), 2.62 (s, 3H), 2.91 (s, 3H), other signals masked by major conformer. ^{13}C NMR ($CDCl_3$, 125 MHz) δ major conformer: 15.2 (CH_3), 15.3 (CH_3), 16.1 (CH_3), 36.8 (CH_3), 52.9 (CH_2), 123.9 (CH), 124.3 (CH), 125.8 (CH), 126.1 (CH), 126.5 (CH), 127.2 (CH), 127.4 (CH), 127.5 (CH), 127.8 (CH), 127.9 (CH), 128.7 (CH), 128.6 (CH), 128.9 (CH), 129.2 (CH), 130.9 (CH), 131.8 (Cq), 135.8 (Cq), 135.9 (Cq), 137.0 (Cq), 137.1 (Cq), 137.4 (Cq), 138.6 (Cq), 139.8 (Cq), 141.7 (Cq), 142.7 (Cq), 151.0 (Cq), 166.2 (Cq), 169.6 (Cq), 170.5 (Cq). MS (ESI$^+$) *m/z*: 644 (21) [M+NH_4], 649 (100) [M+Na]. HRMS calcd for $C_{38}H_{38}N_5O_5$: 644.2867, found: 644.2876. Mp=100–102 °C.

4.3.29. 1-N,3-N-Dibenzyl-2-methyl-1-N-{2-methyl-3-[(2-methyl-3-nitrobenzene)amido]benzene}-3-N-phenylbenzene-1,3-dicarboxamide ***7c'***. Prepared according to general procedure B from nitro **6c'** (53.0 mg, 0.093 mmol), $SnCl_2\cdot 2H_2O$ (210 mg, 0.931 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 5/5) to afford a white solid (49 mg, 98%). IR (film) 3460–3360, 1643, 1592, 1391, 730 cm^{-1}. Ratio: 95/5. ^{1}H NMR ($CDCl_3$, 300 MHz) δ major conformer: 2.01 (s, 3H), 2.27 (s, 3H), 3.39 (br s, 2H), 3.92 (br m, 1H), 5.01 (d, *J*=14.4 Hz, 1H), 5.05 (d, *J*=14.4 Hz, 1H), 5.64 (d, *J*=13.9 Hz, 1H), 6.22 (br m, 1H), 6.28 (d, *J*=7.6 Hz, 1H), 6.39 (d, *J*=7.9 Hz, 1H), 6.51 (t, *J*=7.6 Hz, 1H), 6.64 (t, *J*=7.9 Hz, 1H), 6.66–6.71 (m, 2H), 6.73 (d, *J*=7.5 Hz, 1H), 6.98–7.11 (m, 5H), 7.14–7.20 (m, 2H), 7.22–7.31 (m, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ major conformer: 14.4 (CH_3), 15.4 (CH_3), 51.8 (CH_2), 52.9 (CH_2), 115.3 (CH), 119.0 (Cq), 125.3 (CH), 125.9 (CH), 127.0 (CH), 127.1 (CH), 127.5 (CH), 127.6 (CH), 127.6 (CH), 128.3 (CH), 128.6 (CH), 128.7 (CH), 129.2 (CH), 129.6 (CH), 130.3 (CH), 132.3 (Cq), 136.7 (Cq), 136.9 (Cq), 137.3 (Cq), 138.0 (Cq), 140.9 (Cq), 141.9 (Cq), 144.8 (Cq), 169.8 (Cq), 171.2 (Cq). MS (ESI$^+$) *m/z*: 562 (100) [M+Na]. HRMS calcd for $C_{36}H_{33}N_3NaO_2$: 562.2465, found: 562.2469.

This method was used to make the title compound by general procedure A from acid (34.0 mg, 0.188 mmol), oxalyl chloride (0.08 mL, 0.945 mmol), amine (49 mg, 0.091 mmol) and Et_3N (0.026 mL, 0.186 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 5/5) to afford a white solid (43 mg, 67%). IR (film) 3257, 1645, 1527 cm^{-1}. Ratio: 83/17. ^{1}H NMR ($CDCl_3$, 300 MHz) δ major conformer: 2.14 (s, 3H), 2.28 (s, 3H), 2.59 (s, 3H), 3.95 (d, *J*=13.5 Hz, 1H), 5.01–5.21 (br m, 2H), 5.55 (d, *J*=13.5 Hz, 1H), 6.26 (d, *J*=6.8 Hz, 1H), 6.59–6.68 (m, 2H), 6.72–6.79 (m, 2H), 6.80–6.93 (m, 2H), 6.98–7.06 (m, 2H), 7.07–37 (m, 11H), 7.41 (t, *J*=7.8 Hz, 1H), 7.57 (d, *J*=7.4 Hz, 1H), 7.67 (d, *J*=7.9 Hz, 1H), 7.91 (d, *J*=7.8 Hz, 1H), 7.98 (s, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ major conformer: 15.3 (CH_3), 15.5 (CH_3), 16.4 (CH_3), 52.3 (CH_2), 53.3 (CH_2), 123.6 (CH), 124.5 (CH), 124.6 (CH), 125.7 (CH), 125.8 (CH), 125.9 (CH), 126.1 (CH), 127.1 (CH), 127.5 (CH), 127.9 (CH), 128.1 (CH), 128.6 (CH), 128.8 (CH), 128.9 (CH), 129.2 (CH), 129.7 (CH), 130.5 (CH), 130.9 (Cq), 131.0 (CH), 132.3 (Cq), 136.0 (Cq), 136.6 (Cq), 137.2 (Cq), 137.5 (Cq), 138.7 (Cq), 140.1 (Cq), 140.6 (Cq), 142.1 (Cq), 151.2 (Cq), 166.5 (Cq), 169.9 (Cq), 170.5 (Cq). MS (ESI$^+$) *m/z*: 725 (100) [M+Na]. HRMS calcd for $C_{44}H_{38}N_4NaO_5$: 725.2734, found: 725.2734.

4.3.30. 1-N-Benzyl-2,3-N-dimethyl-3-N-{2-[(2-methyl-3-nitrobenzene)amido]benzene}-1-N-phenylbenzene-1,3-dicarboxamide ***7d***. Prepared according to general procedure B from nitro **6d** (100 mg, 0.209 mmol), $SnCl_2\cdot 2H_2O$ (470 mg, 2.09 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 6/4) to afford a yellow foam (91 mg, 97%). IR (film) 3457, 3356, 3032, 1641, 1591 cm^{-1}. Ratio: 94/6. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.29 (s, 3H), 3.20 (s, 3H), 4.62 (br s, 2H), 5.03 (d, *J*=14.3 Hz, 1H), 5.16 (d, *J*=14.3 Hz, 1H), 6.15 (m, 1H), 6.43 (m, 1H), 6.57 (d, *J*=8.1 Hz, 1H), 6.76–6.69 (m, 2H), 6.88–6.79 (m, 3H), 6.93 (m, 1H), 7.04 (m, 3H), 7.36–7.23 (m, 5H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 15.0 (CH_3), 37.2 (CH_3), 52.9 (CH_2), 116.4 (CH), 116.5 (CH), 118.7 (CH), 126.1 (CH), 126.5 (CH), 127.0 (CH), 127.5 (CH), 128.4 (CH), 128.6 (CH), 128.8 (CH), 130.4 (Cq), 130.5 (Cq), 131.8 (CH), 137.2 (Cq), 138.4 (Cq), 141.8 (Cq), 144.3 (Cq), 146.8 (Cq), 169.9 (Cq), 171.1 (Cq). MS (ESI$^+$) *m/z*: 472 (100) [M+Na]. HRMS calcd for $C_{29}H_{27}N_3NaO_2$: 472.1995, found: 472.2003. Mp=128–130 °C.

This amine was used to make the title compound according to general procedure A from acid (73.0 mg, 0.403 mmol), oxalyl chloride (0.17 mL, 2.01 mmol), amine (90.0 mg, 0.200 mmol) and pyridine (0.048 mL, 0.593 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 6/4 to EtOAc) to afford a white solid (89 mg, 73%). IR (film) 3032, 1641, 1526 cm^{-1}. Ratio: 95/5. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.22 (s, 3H), 2.63 (s, 3H), 3.20 (s, 3H), 5.05 (d, *J*=14.6 Hz, 1H), 5.09 (d, *J*=14.6 Hz, 1H), 6.60 (m, 2H), 6.71 (m, 2H), 6.78 (d, *J*=7.6 Hz, 1H), 6.84–6.96 (m, 2H), 7.01–7.10 (m, 4H), 7.18–7.37 (m, 5H), 7.45 (t, *J*=7.8 Hz, 1H), 7.73 (d, *J*=7.5 Hz, 1H), 7.91 (d, *J*=7.8 Hz, 1H), 8.39 (d, *J*=8.4 Hz, 1H), 10.1 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.9 (CH_3), 16.1 (CH_3), 37.8 (CH_3), 53.0 (CH_2), 122.0 (CH), 122.9 (CH), 125.6 (CH), 126.5 (CH), 127.0 (CH), 127.1 (CH), 127.2 (CH), 127.6 (CH), 128.4 (CH), 128.5 (CH), 128.6 (CH), 128.9 (CH), 129.0 (CH), 130.7 (CH), 130.7 (Cq), 130.9 (CH), 131.4 (Cq), 137.0 (Cq), 137.2 (Cq), 138.9 (Cq), 139.8 (Cq), 141.6 (Cq), 143.6 (Cq), 151.1 (Cq), 170.1 (Cq), 169.5 (Cq), 165.9 (Cq). MS (ESI$^+$) *m/z*: 630 (100) [M+NH_4]. HRMS calcd for $C_{37}H_{36}N_5O_5$: 630.2711, found: 630.2720. Mp=144–145 °C.

4.3.31. 1-N-Benzyl-2,3-N-dimethyl-3-N-{4-[(2-methyl-3-nitrobenzene)amido]benzene}-1-N-phenylbenzene-1,3-dicarboxamide ***7e***. Prepared according to general procedure B from nitro **6e** (79.0 mg, 0.164 mmol), $SnCl_2\cdot 2H_2O$ (370 mg, 1.64 mmol) in DMF (3 mL). The crude mixture was purified through silica gel (PE/EtOAc: 4/6) to afford a white foam (65.5 mg, 89%). IR (film) 3351, 3047, 1633, 1605 cm^{-1}. Ratio: >95/5. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.20 (s, 3H), 3.12 (s, 3H), 3.63 (br s, 2H), 5.02 (d, *J*=14.2 Hz, 1H), 5.12 (d, *J*=14.2 Hz, 1H), 6.23 (d, *J*=7.9 Hz, 2H), 6.73 (d, *J*=7.0 Hz, 2H), 6.77 (m, 1H), 6.83 (m, 1H), 6.91 (m, 3H), 7.04 (m, 3H), 7.22–7.28 (m, 5H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 15.2 (CH_3), 37.9 (CH_3), 53 (CH_2), 113.6 (CH), 124.6 (Cq), 126.3 (CH), 126.5 (CH), 127.2 (CH), 127.6 (CH), 127.7 (CH),

128.5 (CH), 128.7 (CH), 128.9 (CH), 129.0 (CH), 130.5 (CH), 131.2 (Cq), 137.2 (Cq), 138.8, (Cq), 141.8 (Cq), 144.9 (Cq), 148.0 (Cq), 170.1 (Cq), 170.5 (Cq). MS (ESI^+) *m/z*: 472 (30) [M+Na]. HRMS calcd for $C_{29}H_{27}N_3NaO_2$: 472.1995, found: 472.2001.

The title compound was made using general procedure A from acid (59.4 mg, 0.328 mmol), oxalyl chloride (0.14 mL, 1.64 mmol), this amine (65.5 mg, 0.145 mmol) and pyridine (0.03 mL, 0.371 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 4/6) to afford a white solid (80 mg, 90%). IR (film) 3255, 3057, 1643, 1528 cm^{-1}. Ratio: 90/10. ^1H NMR (DMSO-d_6, 300 MHz) δ 2.22 (s, 3H), 2.51 (s, 3H), 3.08 (s, 3H), 5.00 (br m, 2H), 6.79 (m, 3H), 6.91 (m, 2H), 7.00 (d, *J*=8.1 Hz, 2H), 7.20–7.10 (m, 3H), 7.37–7.23 (m, 6H), 7.83 (d, *J*=7.8 Hz, 1H), 7.60 (d, *J*=7.6 Hz, 1H), 7.41 (d, *J*=8.4 Hz, 2H), 9.27 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 15.1 (CH_3), 16.0 (CH_3), 37.6 (CH_3), 52.8 (CH_2), 118.5 (CH), 125.2 (CH), 126.4 (CH), 126.6 (CH), 126.9 (CH), 127.6 (CH), 127.6 (CH), 128.5 (CH), 128.5 (CH), 128.9 (CH), 129.3 (CH), 130.4 (Cq), 130.5 (Cq), 130.8 (CH), 131.5 (Cq), 136.9 (Cq), 138.6 (Cq), 139.6 (Cq), 139.9 (Cq), 141.2 (Cq), 143.8 (Cq), 150.6 (Cq), 166.4 (Cq), 169.8 (Cq), 169.9 (Cq). MS (ESI^+) *m/z*: 635 (100) [M+Na]. HRMS calcd for $C_{37}H_{32}N_4NaO_5$: 635.2265, found: 635.2267. Mp=104–106 °C.

4.3.32. 1-N,2,3-N-Trimethyl-1-N-{2-methyl-3-[methyl(2-methyl-3-nitrobenzene)amido]benzene}-3-N-phenylbenzene-1,3-dicarboxamide ***8c****.* Prepared according to general procedure C from amide **7c** (65.0 mg, 0.118 mmol), NaH (19.0 mg, 0.475 mmol) and MeI (0.07 mL, 1.18 mmol). The crude mixture was purified through silica gel (PE then PE/EtOAc 8/2 to 1/9) to afford a colourless foam (*m*=48 mg, 72%). ^1H NMR and ^{13}C NMR show mixture of multiple conformers resulting impossible to determine any ratio. MS (CI) *m/z*: 565 (30) [M+H]. HRMS calcd for $C_{33}H_{33}N_4O_5$: 565.2445, found: 565.2436.

4.3.33. 1-N-Benzyl-2,3-N-dimethyl-3-N-{2-methyl-3-[methyl(2-methyl-3-nitrobenzene)amido]benzene}-1-N-phenylbenzene-1,3-dicarboxamide ***8c′****.* Prepared according to general procedure C from amide **7c′** (46.0 mg, 0.073 mmol), NaH (12.0 mg, 0.300 mmol) and MeI (0.046 mL, 0.739 mmol). The crude mixture was purified through silica gel (PE then PE/EtOAc 9/1 to 2/8) to afford a colourless foam (*m*=36 mg, 77%). ^1H NMR and ^{13}C NMR show mixture of multiple conformers resulting impossible to determine any ratio. MS (ESI^+) *m/z*: 663 (100) [M+Na]. HRMS calcd for $C_{39}H_{36}N_4NaO_5$: 663.2578, found: 663.2577.

4.3.34. 1-N,3-N-Dibenzyl-1-N-{3-[benzyl(2-methyl-3-nitrobenzene)amido]-2-methylbenzene}-2-methyl-3-N-phenylbenzene-1,3-dicarboxamide ***8c'****.* Prepared according to general procedure C from amide **7c'** (40.0 mg, 0.057 mmol), NaH (9.00 mg, 0.225 mmol), benzyl bromide (0.07 mL, 0.589 mmol). The crude mixture was purified through silica gel (PE to PE/EtOAc: 6/4) to afford a white solid (*m*=42 mg, 93%). ^1H NMR and ^{13}C NMR show mixture of multiple conformers resulting impossible to determine any ratio. MS (ESI^+) *m/z*: 810 (62) [M+NH_4], 815 (100) [M+Na]. HRMS calcd for $C_{51}H_{44}N_4NaO_5$: 815.3204, found: 815.3182.

4.3.35. 1-N-Benzyl-2,3-N-dimethyl-3-N-{2-[methyl(2-methyl-3-nitrobenzene)amido]benzene}-1-N-phenylbenzene-1,3-dicarboxamide ***8d****.* Prepared according to general procedure C from amide **7d** (56.0 mg, 0.091 mmol), NaH (14.6 mg, 0.365 mmol), methyl iodide (0.06 mL, 0.963 mmol). The crude mixture was purified through silica gel (PE to PE/EtOAc: 6/4) to afford a white solid (41 mg, 72%). ^1H NMR and ^{13}C NMR show mixture of multiple conformers resulting impossible to determine any ratio. MS (ESI^+) *m/z*: 649 (100) [M+Na]. HRMS calcd for $C_{38}H_3N_4NaO_5$: 649.2421, found: 649.2415.

4.3.36. 1-N-Benzyl-2,3-N-dimethyl-3-N-{4-[methyl(2-methyl-3-nitrobenzene)amido]benzene}-1-N-phenylbenzene-1,3-dicarboxamide ***8e****.* Prepared according to general procedure C from amide **7e** (77.0 mg, 0.125 mmol), NaH (20.0 mg, 0.500 mmol), methyl iodide (0.08 mL, 1.25 mmol). The crude mixture was purified through silica gel (PE to PE/EtOAc: 6/4) to afford a yellow solid (56 mg, 72%). ^1H NMR ($CDCl_3$, 300 MHz) δ 2.24 (br s, 3H), 2.34 (br s, 3H), 3.09 (br s, 3H), 3.42 (br s, 3H), 5.11 (br m, 2H), 6.48 (br m, 1H), 6.69 (br m, 3H), 6.84 (br m, 2H), 6.94 (br m, 3H), 7.03–7.15 (br m, 5H), 7.26–7.34 (br m, 5H), 7.69 (br m, 1H). MS (ESI^+) *m/z*: 649 [M+Na]. HRMS calcd for $C_{38}H_{34}N_4NaO_5$: 649.2421, found: 649.2434.

4.3.37. tert-Butyl 3-(N-benzyl-2-methyl-3-nitrobenzamido)-2-methylbenzoate ***12****.* Pyridine (2 mL) and *t*-BuOH (2 mL) were added to a flask containing the acid chloride (200 mg, 1.00 mmol). The solution was then stirred overnight at rt. After addition of DCM, the resulting solution was washed with water, 5% HCl then brine. The organic layer was dried over Na_2SO_4 and the solvent removed under vacuo. Purification of the crude mixture through silica gel (PE/EtOAc: 9/1) affords the product as a colourless oil (*m*=54 mg, 23%). ^1H NMR ($CDCl_3$, 300 MHz) δ 1.60 (s, 9H), 2.59 (s, 3H), 7.35 (t, *J*=7.8 Hz, 1H), 7.81 (dd, *J*=8.1, 1.1 Hz, 1H), 7.86 (dd, *J*=7.8, 1.1 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.0 (Cq), 151.7 (Cq), 135.7 (Cq), 133.0 (CH), 132.0 (Cq), 126.3 (CH), 126.0 (CH), 82.7 (Cq), 28.1 (CH_3), 16.2 (CH_3). MS (ESI^+) *m/z*: 255 (50) [M+H]. HRMS calcd for $C_{12}H_{19}N_2O_4$: 255.1339, found: 255.1340.

Nitro compound was reduced according to general procedure B from nitroarene (32.0 mg, 0.135 mmol), $SnCl_2\cdot 2H_2O$ (304 mg, 1.35 mmol). The crude mixture was used without further purification. Secondary amide was prepared according to general procedure A from acid (49.0 mg, 0.270 mmol), oxalyl chloride (0.12 mL, 1.35 mmol), previous amine (0.135 mmol) and Et_3N (0.04 mL, 0.287 mmol). Benzylation was made according to procedure C from amide (40.0 mg, 0.108 mmol), NaH (18.0 mg, 0.432 mmol) and BnBr (0.13 mL, 1.08 mmol). The crude mixture was purified through silica gel (PE then PE/EtOAc 9/1) to afford a colourless oil (*m*=42 mg, 63% over three steps). IR (film) 3067–2933, 1714, 1650 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 1.54 (s, 9H), 2.45 (s, 3H), 2.47 (s, 3H), 4.16 (d, *J*=13.7 Hz, 1H), 5.75 (d, *J*=13.7 Hz, 1H), 6.86 (t, *J*=7.8 Hz, 1H), 7.04 (t, *J*=7.8 Hz, 1H), 7.14 (m, 1H), 7.21–7.30 (m, 6H), 7.55 (dd, *J*=7.8, 1.3 Hz, 1H), 7.62 (dd, *J*=8.0, 1.3 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 16.0 (CH_3), 16.7 (CH_3), 28.2 (CH_3), 52.4 (CH_2), 81.9 (Cq), 124.6 (CH), 125.8 (CH), 126.1 (CH), 128.0 (CH), 128.5 (CH), 129.6 (CH), 129.7 (CH), 130.1 (Cq), 130.3 (CH), 132.6 (CH), 133.9 (Cq), 136.1 (Cq), 136.2 (Cq), 139.2 (Cq), 140.6 (Cq), 150.2 (Cq), 166.3 (Cq), 168.7 (Cq). MS (ESI^+) *m/z*: 483 (60) [M+Na]. HRMS calcd for $C_{27}H_{28}N_2NaO_5$: 483.1890, found: 483.1897.

4.3.38. 3-N-Benzene-1-N-benzyl-2-methyl-1-N-phenylbenzene-1,3-dicarboxamide ***13****.* Prepared according to general procedure A from benzoyl chloride (0.15 mL, 1.26 mmol), amine derived from **4c′** (209 mg, 0.661 mL) and Et_3N (0.18 mL, 1.26 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 6/4) to afford a white solid (256 mg, 93%). IR (film) 3288, 3062–3032, 1649 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 2.32 (s, 3H), 5.14 (s, 2H), 6.86 (m, 3H), 7.00 (t, *J*=7.8 Hz, 1H), 7.08 (m, 3H), 7.34–7.27 (m, 4H), 7.48 (m, 2H), 7.55 (m, 1H), 7.62 (m, 1H), 7.83 (m, 3H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.7 (CH_3), 52.9 (CH_2), 124.2 (CH), 124.4 (CH), 125.6 (CH), 127.2 (CH), 127.4 (CH), 127.5 (CH), 127.7 (Cq), 128.4 (CH), 128.5 (CH), 128.5 (CH), 128.8 (CH), 131.6 (CH), 134.5 (Cq), 136.2 (Cq), 137.1 (Cq), 141.7 (Cq), 166.7 (Cq), 170.7 (Cq). MS (ESI^+) *m/z*: 443 (100) [M+Na]. HRMS calcd for $C_{28}H_{24}N_2NaO_2$: 443.1730, found: 443.1732. Mp=152–154 °C.

The secondary amide was alkylated according to general procedure C using amide (57.0 mg, 0.136 mmol), NaH (22.0 mg, 0.550 mmol), methyl iodide (0.084 mL, 1.36 mmol). The crude mixture was purified through silica gel (PE then PE/EtOAc: 6/4) to afford a white solid (50 mg, 85%). IR (film) 3062, 1644, 1593 cm^{-1}. Ratio: >95/5. ^1H NMR ($CDCl_3$, 300 MHz) δ 2.27 (s, 3H), 3.21 (s, 3H), 5.03 (d, *J*=14.4 Hz, 1H), 5.14 (d, *J*=14.4 Hz, 1H), 6.73 (m, 2H), 6.81 (m,

2H), 6.90 (m, 1H), 7.13–7.01 (m, 7H), 7.20 (m, 1H), 7.28 (m, 5H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 15.1 (CH_3), 37.5 (CH_3), 52.9 (CH_2), 126.1 (CH), 126.8 (CH), 127.1 (CH), 127.5 (CH), 127.6 (CH), 127.6 (CH), 128.1 (CH) 128.5 (CH), 128.6 (CH), 128.9 (CH), 129.0 (CH), 129.6 (CH), 131.8 (Cq), 135.3 (Cq), 137.1 (Cq), 138.7 (Cq), 141.7 (Cq), 144.0 (Cq), 169.8 (Cq), 170.5 (Cq). MS (ESI$^+$) *m/z*: 457 (100) [M+Na]. HRMS calcd for $C_{29}H_{26}N_2NaO_2$: 457.1886, found: 457.1900. Mp=114–116 °C.

4.3.39. N-{3-[Benzene(methyl)amido]-2-methylphenyl}-N-methylbenzamide ***17a***. Prepared according to general procedure A from benzoyl chloride (1.68 mL, 13.1 mmol), amine **16** (1.00 g, 6.57 mmol) and pyridine (1.6 mL, 19.7 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 7/3 then EtOAc) to afford a white solid (1.49 g, 89%). IR (film) 3266, 1645, 1522 cm^{-1}. ^{1}H NMR (DMSO-d_6, 300 MHz) δ 2.31 (s, 3H), 7.48 (m, 1H), 7.58–7.52 (m, 2H), 7.65–7.59 (m, 1H), 7.69 (dd, *J*=7.9, 1.1 Hz, 1H), 7.82 (dd, *J*=8.1, 1.2 Hz, 1H), 8.03 (m, 2H), 10.3 (br s, 1H). ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ 14.0 (CH_3), 121.5 (CH), 126.6 (CH), 127.7 (CH), 128.3 (Cq), 128.4 (CH), 131.3 (CH), 131.8 (CH), 133.8 (Cq), 138.4 (Cq), 150.8 (Cq), 165.6 (Cq). MS (ESI$^+$) *m/z*: 257 (100) [M+H], 279 (15) [M+Na]. HRMS calcd for $C_{14}H_{13}N_2O_3$: 257.0921, found: 257.0924. Mp=164–165 °C.

The amide was alkylated according to general procedure C using amide (150 mg, 0.586 mmol), NaH (93.0 mg, 2.32 mmol), methyl iodide (0.36 mL, 5.78 mmol). The crude mixture was purified through silica gel (PE then PE/EtOAc: 8/2) to afford a yellow solid (143 mg, 92%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.44 (s, 3H), 3.38 (s, 3H), 7.29–7.13 (m, 7H), 7.74 (d, *J*=7.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.5 (CH_3), 37.5 (CH_3), 123.5 (CH), 127.0 (CH), 127.8 (CH), 127.9 (CH), 130.1 (CH), 130.3 (Cq), 133.3 (CH), 134.9 (Cq), 146.6 (Cq), 150.9 (Cq), 170.8 (Cq). MS (ESI$^+$) *m/z*: 271 (100) [M+H]. HRMS calcd for $C_{15}H_{15}N_2O_3$: 271.1077, found: 271.1068. Mp=70–71 °C.

This nitro compound was reduced according to general procedure B using nitro (142 mg, 0.526 mmol), $SnCl_2\cdot 2H_2O$ (1.17 g, 5.18 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 7/3) to afford a white solid (112 mg, 90%). IR (film) 3356, 1628, 1574 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.00 (s, 3H), 3.37 (s, 3H), 3.62 (br s, 2H), 6.52 (m, 2H), 6.89 (t, *J*=7.9 Hz, 1H), 7.27–7.11 (m, 3H), 7.35–7.30 (m, 2H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 11.8 (CH_3), 37.6 (CH_3), 113.9 (CH), 118.3 (CH), 118.9 (Cq), 126.8 (CH), 127.3 (CH), 127.9 (CH), 129.4 (CH), 135.9 (Cq), 143.9 (Cq), 145.8 (Cq), 170.8 (Cq). MS (ESI$^+$) *m/z*: 263 (10) [M+Na]. HRMS calcd for $C_{15}H_{16}N_2NaO_1$: 263.1155, found: 263.1157. Mp=130–131 °C.

This amine was acylated according to general procedure A using benzoyl chloride (0.112 mL, 0.874 mmol), amine (105 mg, 0.437 mmol) and pyridine (0.106 mL, 1.31 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 7/3) to afford a white foam (142 mg, 95%). IR (film) 3287, 3059–2926, 1647 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.15 (s, 3H), 3.29 (s, 3H), 6.87 (d, *J*=7.7 Hz, 1H), 7.12–7.02 (m, 3H), 7.16 (d, *J*=7.1 Hz, 1H), 7.23 (m, 2H), 7.40 (m, 2H), 7.51 (t, *J*=7.3 Hz, 1H), 7.61 (d, *J*=7.9 Hz, 1H), 7.83 (d, *J*=7.3 Hz, 2H), 8.10 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 12.7 (CH_3), 37.6 (CH_3), 123.3 (CH), 125.6 (CH), 126.8 (CH), 127.0 (CH), 127.5 (CH), 127.8 (Cq), 127.9 (CH), 128.6 (CH), 129.6 (CH), 131.8 (CH), 134.3 (Cq), 135.4 (Cq), 137.1 (Cq), 143.9 (Cq), 165.7 (Cq), 170.8 (Cq). MS (ESI$^+$) *m/z*: 367 (100) [M+Na]. HRMS calcd for $C_{22}H_{20}N_2NaO_2$: 367.1417, found: 367.1429. Mp=52–54 °C.

This amide was alkylated according to general procedure C using amide (142 mg, 0.413 mmol), NaH (66.0 mg, 1.65 mmol), methyl iodide (0.26 mL, 4.13 mmol). The crude mixture was purified through silica gel (PE then PE/EtOAc: 6/4) to afford a white solid (123 mg, 83%). IR (film) 3060–2929, 1644, 1574, 1362 cm^{-1}. Ratio: 2/1. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.98 (s, 3H, min), 2.19 (s, 3H, maj), 3.12 (s, 6H, min), 3.29 (s, 6H, maj), 7.62–6.81 (m, 13H, maj+min). ^{13}C NMR ($CDCl_3$, 75.5 MHz) major conformer δ 13.1 (CH_3), 37.7 (CH_3), 127.1 (CH), 127.2 (CH), 127.5 (CH), 127.6 (CH), 127.9 (CH), 128.0 (CH), 128.3 (CH), 129.7 (CH), 132.1 (Cq), 135.2 (Cq), 145.1 (Cq), 170.5 (Cq). Minor conformer δ 13.5 (CH_3), 37.2 (CH_3), 132.2 (Cq), 135.4 (Cq), 145.0 (Cq), 170.3 (Cq) other signals masked by major conformer. MS (ESI$^+$) *m/z*: 359 (100) [M+H], 376 (84) [M+NH_4], 381 (57) [M+Na]. HRMS calcd for $C_{23}H_{26}N_3O_2$: 376.2020, found: 376.2027. Mp=128–130 °C.

4.3.40. N-{3-[Benzene(benzyl)amido]-2-methylphenyl}-N-benzylbenzamide ***17b***. Prepared according to general procedure C from the benzamide derived from **16** (150 mg, 0.586 mmol), NaH (93.0 mg, 2.32 mmol), benzyl bromide (0.69 mL, 5.81 mmol). The crude mixture was purified through silica gel (PE then PE/EtOAc: 8/2) to afford a colourless oil (112 mg, 56%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.23 (s, 3H), 4.63 (d, *J*=14.0 Hz, 1H), 5.51 (d, *J*=14.0 Hz, 1H), 7.22–7.06 (m, 4H), 7.35–7.24 (m, 8H), 7.74 (d, *J*=7.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.4 (CH_3), 53.0 (CH_2), 123.7 (CH), 126.4 (CH), 127.8 (CH), 127.8 (CH), 127.9 (CH), 128.5 (CH), 129.3 (CH), 130.0 (CH), 131.0 (Cq), 134.5 (CH), 135.1 (Cq), 135.9 (Cq), 143.4 (Cq), 150.8 (Cq), 170.3 (Cq). MS (ESI$^+$) *m/z*: 347 (46) [M+H], 364 (48) [M+NH_4], 369 (70) [M+Na]. HRMS calcd for $C_{21}H_{19}N_2O_3$: 347.1390, found: 347.1382.

This nitro compound was reduced according to general procedure B using nitro (112 mg, 0.323 mmol), $SnCl_2\cdot 2H_2O$ (722 mg, 3.20 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 7/3) to afford a white solid (93 mg, 92%). IR (film) 3469, 1631 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.67 (s, 3H), 3.40 (br s, 2H), 4.76 (d, *J*=13.9 Hz, 1H), 5.25 (d, *J*=13.9 Hz, 1H), 6.41 (dd, *J*=7.8, 0.8 Hz, 1H), 6.48 (dd, *J*=7.9, 0.8 Hz, 1H), 6.84 (dt, *J*=7.9, 0.4 Hz, 1H), 7.15–7.08 (m, 2H), 7.19 (m, 1H), 7.28–7.24 (m, 3H), 7.36–7.29 (m, 4H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 11.9 (CH_3), 53.5 (CH_2), 114.0 (CH), 119.4 (CH), 119.9 (Cq), 126.5 (CH), 127.3 (CH), 128.0 (CH), 128.1 (CH), 129.3 (CH), 129.4 (CH), 136.1 (Cq), 136.9 (Cq), 142.1 (Cq), 145.6 (Cq), 170.3 (Cq). MS (ESI$^+$) *m/z*: 317 (28) [M+H], 339 (61) [M+Na]. HRMS calcd for $C_{21}H_{20}N_2NaO_1$: 339.1468, found: 339.1473. Mp=136–138 °C.

This amine was acylated according to general procedure A using benzoyl chloride (0.089 mL, 0.767 mmol), amine (84.0 mg, 0.265 mmol) and pyridine (0.085 mL, 1.05 mmol). The crude mixture was purified through silica gel (PE/EtOAc: 8/2) to afford a white foam (132 mg, 90%). IR (film) 3293, 3060, 1647 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.92 (s, 3H), 4.77 (d, *J*=13.9 Hz, 1H), 5.35 (d, *J*=14.3 Hz, 1H), 6.85 (d, *J*=7.9 Hz, 1H), 7.20–7.09 (m, 3H), 7.24 (m, 1H), 7.38–7.29 (m, 7H), 7.49 (m, 2H), 7.58 (m, 1H), 7.68 (br s, 1H), 7.85 (m, 3H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 12.6 (CH_3), 53.5 (CH_2), 122.4 (CH), 126.3 (CH), 126.7 (CH), 126.9 (CH), 127.2 (Cq), 127.6 (CH), 128.1 (CH), 128.3 (CH), 128.7 (CH), 129.4 (CH), 129.7 (CH), 131.9 (CH), 134.5 (Cq), 135.7 (Cq), 136.6 (Cq), 137.0 (Cq), 142.1 (Cq), 165.5 (Cq), 170.4 (Cq). MS (ESI$^+$) *m/z*: 443 (100) [M+Na]. HRMS calcd for $C_{28}H_{24}N_2NaO_2$: 443.1730, found: 443.1727.

This amide was benzylated according to general procedure C using amide (76.0 mg, 0.181 mmol), NaH (29.0 mg, 0.724 mmol), benzyl bromide (0.22 mL, 1.81 mmol). The crude mixture was purified through silica gel (PE then PE/EtOAc: 8/2) to afford a white solid (73 mg, 79%). IR (film) 3061, 1644, 1381 cm^{-1}. Ratio: 2/1. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.70 (s, 3H, maj), 1.72 (s, 3H, min), 4.23 (d, *J*=4.3 Hz, 1H, maj), 4.51 (d, *J*=13.9 Hz, 1H, min), 5.18 (d, *J*=13.8 Hz, 1H, maj), 5.26 (d, *J*=13.9 Hz, 1H, min), 6.64 (d, *J*=7.9 Hz, 1H, maj), 6.69 (d, *J*=7.8 Hz, 1H, min), 6.82 (m, 1H, min), 7.15–7.02 (m, 4H, maj+min), 7.38–7.18 (m, 12H, maj+min). ^{13}C NMR ($CDCl_3$, 75.5 MHz) major conformer δ 13.5 (CH_3), 52.6 (CH_2), 126.4 (CH), 127.5 (CH), 127.6 (CH), 128.1 (CH), 128.2 (CH), 129.3 (CH), 129.5 (CH), 129.8 (CH), 133.7 (Cq), 135.8 (Cq), 136.2 (Cq), 142.7 (Cq), 170.0 (Cq). Minor conformer δ 13.2 (CH_3), 53.1 (CH_2), 127.7 (CH), 128.0 (CH), 128.2 (CH), 129.7 (CH), 129.7 (CH), 134.1 (Cq), 135.4 (Cq), 136.3 (Cq), 142.6 (Cq), other signals masked by major conformer. MS (ESI$^+$) *m/z*: 511 (100) [M+H], 528 (43) [M+NH_4], 533 (22) [M+Na]. HRMS calcd for $C_{35}H_{31}N_2O_2$: 511.2380, found: 511.2392. Mp=169–170 °C.

4.3.41. N-Methyl-4-nitro-N-phenylbenzamide ***18a***. Prepared according to general procedure A from 4-nitrobenzoyl chloride (1.50 g,

8.08 mmol), pyridine (2.2 mL, 27.2 mmol) and *N*-methylaniline (0.86 mL, 7.94 mmol), **18a** was obtained without further purification (2.03 g, 98%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.55 (s, 3H), 7.06 (d, J=7.2 Hz, 2H), 7.23 (t, J=6.9 Hz, 1H), 7.27 (dd, J=7.2, 6.9 Hz, 2H), 7.48 (d, J=8.7 Hz, 2H), 8.04 (d, J=8.7 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 38.2 (CH_3), 122.9 (CH), 126.9 (CH), 127.3 (CH), 129.5 (CH), 142.1 (Cq), 143.7 (Cq), 147.9 (Cq), 168.3 (Cq). IR (film) 1651, 1520 cm^{-1}. HRMS calcd for $C_{14}H_{13}N_2O_3$: 257.0921, found: 257.0925. Anal. Calcd for $C_{14}H_{12}N_2O_3\cdot$¼H_2O (260.76): C, 64.49; H, 4.83; N, 10.74. Found: C, 64.79; H, 4.62; N, 10.74.

4.3.42. 2-Iodo-N-methyl-N-(4-(N′-methyl-N′-phenyl)carbamoyl) phenylbenzamide ***19a′***. Prepared according to general procedure B from **18a** (2.00 g, 7.81 mmol) and $SnCl_2\cdot 2H_2O$ (17.5 g, 77.5 mmol), the amine was obtained without further purification (1.7 g, 96%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.38 (br s, 2H), 3.46 (s, 3H), 6.40 (d, J=8.7 Hz, 2H), 7.04 (dd, J=7.5, 1.5 Hz, 2H), 7.11–7.15 (m, 1H), 8.13 (d, J=8.7 Hz, 2H), 7.24 (dd, J=7.5, 7.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 38.6 (CH_3), 113.6 (CH), 125.3 (Cq), 126.0 (CH), 127.8 (CH), 129.1 (CH), 131.1 (CH), 145.8 (Cq), 147.8 (Cq), 170.5 (Cq). IR (film) 3350, 1630 cm^{-1}. HRMS calcd for $C_{14}H_{14}N_2NaO$: 249.0998, found: 249.1002. Anal. Calcd for $C_{14}H_{14}N_2O\cdot$¼H_2O (230.78): C, 72.86; H, 6.33; N, 12.14. Found: C, 73.21; H, 6.15; N, 12.16.

Prepared according to general procedure A from this amine (102 mg, 0.451 mmol), pyridine (0.2 mL, 2.47 mmol) and 2-iodobenzoyl chloride (97%, 142 mg, 0.517 mmol) the amide was obtained without further purification (202 mg, quantitative). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.44 (s, 3H), 7.04 (d, J=7.2 Hz, 1H), 7.07–7.45 (m, 11H), 7.86 (d, J=7.8 Hz, 1H), 7.94 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75,5 MHz) δ 38.6 (CH_3), 92.4 (Cq), 118.8 (CH), 126.6 (CH), 126.8 (CH), 128.2 (CH), 128.4 (CH), 128.3 (CH), 130.0 (CH), 131.4 (CH), 131.5 (Cq), 139.0 (Cq), 139.9 (CH), 141.7 (Cq), 144.8 (Cq), 167.3 (Cq), 169.9 (Cq). IR (film) 3240, 1624, 1594 cm^{-1}. HRMS calcd for $C_{21}H_{18}IN_2O_2$: 457.0407 found: 457.0408.

Prepared according to general procedure C from NaH (60%, 79.0 mg, 1.97 mmol), the amide (224 mg, 0.491 mmol) and iodomethane (0.3 mL, 4.82 mmol). The crude product was purified by flash chromatography (DCM to DCM/MeOH 1%) to yield **19a′** (201 mg, 96%). Mp 210–212 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) major conformer δ 3.41 (s, 3H), 3.42 (s, 3H), 6.83–6.93 (m, 6H), 7.05–7.15 (m, 6H), 7.59 (d, J=7.7 Hz, 1H), Minor conformer δ 3.09 (br s, 6H), other signals masked by major conformer. Ratio 16:1. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 37.0 (CH_3), 38.2 (CH_3), 93.4 (Cq), 126.1 (CH), 126.5 (CH), 126.7 (CH), 127.3 (CH), 128.5 (CH), 129.1 (CH), 129.4 (CH), 129.9 (CH), 134.3 (Cq), 139.0 (CH), 141.9 (Cq), 143.9 (Cq), 144.4 (Cq), 169.5 (Cq), 169.9 (Cq). IR (film) 1643, 1603 cm^{-1}. HRMS calcd for $C_{22}H_{20}IN_2O_2$: 471.0564, found: 471.0576.

4.3.43. N-Methyl-N-(4-(N′-methyl-N′-phenyl)carbamoyl)phenyl-4-nitrobenzamide ***19a***. Prepared according to general procedure A from the amine derived from **18a** (1.60 g, 7.08 mmol) and 4-nitrobenzoyl chloride (1.33 g, 7.17 mmol) a very insoluble amide was obtained without further purification (2.65 g, quantitative). ^{1}H NMR (DMSO-d_6, 300 MHz) δ 3.39 (s, 3H), 7.18–7.21 (m, 3H), 7.26–7.34 (m, 4H), 7.67 (d, J=8.7 Hz, 2H), 8.19 (d, J=8.7 Hz, 2H), 8.37 (d, J=8.7 Hz, 2H), 10.75 (s, 1H). IR (film) 3360, 1635 cm^{-1}. HRMS calcd for $C_{21}H_{18}N_3O_4$: 376.1292, found: 376.1294.

To a solution of this amide (1.15 g, 3.07 mmol) in THF (100 mL) at 0 °C, NaH (480 mg, 12.0 mmol) was added followed by immediate addition of iodomethane (2 mL, 32.1 mmol). The mixture was stirred at 0 °C under nitrogen overnight. HCl (1.5 N) was added to the solution at 0 °C and it was extracted with AcOEt. The organic layer was washed with water, dried, filtered and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (DCM to DCM/MeOH 10%) to yield **19a** (1.01 g, 85%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.44 (s, 6H), 6.81 (d, J=8.5 Hz, 2H), 6.94 (d, J=7.5 Hz, 2H), 7.12 (t, J=7.5 Hz, 1H), 7.17 (d, J=8.5 Hz, 2H), 7.18 (d, J=7.5 Hz, 2H), 7.31 (d, J=9.0 Hz, 2H), 7.96 (d, J=9.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75,5 MHz) δ 38.2 (CH_3), 38.5 (CH_3), 123.3 (CH), 126.3 (CH), 127.0 (CH), 127.2 (CH), 129.5 (CH), 129.7 (CH), 130.1 (CH), 135.2 (Cq), 142.0 (Cq), 144.7 (Cq), 144.9 (Cq), 148.2 (Cq), 168.4 (Cq), 169.6 (Cq). IR (film) 1648, 1522, 1360, 1310 cm^{-1}. HRMS calcd for $C_{22}H_{20}N_3O_4$: 390.1448, found: 390.1450.

4.3.44. 2-Iodo-N-methyl-N-(4-(N′-methyl-N′-(4-(N″-methyl-N″-phenyl)carbamoyl)phenyl)carbamoyl)phenylbenzamide ***20a′***. Prepared according to general procedure B from **19a** (1.20 g, 3.08 mmol) the amine was obtained (860 mg, 78%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.38 (s, 3H), 3.47 (s, 3H), 3.84 (br s, 2H), 6.35 (d, J=8.4 Hz, 2H), 6.81 (d, J=8.4 Hz, 2H), 6.99 (dd, J=8.1, 1.2 Hz, 2H), 7.02 (dd, J=8.4, 1.8 Hz, 2H), 7.14–7.23 (m, 5H). Minor conformer δ 3.40 (s, 3H), 3.50 (s, 3H), 6.66 (d, J=8.7 Hz, 2H), 7.45 (d, J=8.7 Hz, 2H), 7.66 (d, J=8.4 Hz, 2H), other signals masked by major conformer. Ratio 10:1. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 38.2 (CH_3), 28.4 (CH_3), 113.5 (CH), 124.7 (Cq), 125.6 (CH), 126.5 (CH), 126.8 (CH), 129.1 (CH), 129.7 (CH), 131.0 (CH), 133.1 (Cq), 144.7 (Cq), 146.8 (Cq), 148.1 (Cq), 169.7 (Cq), 170.4 (Cq). IR (film) 3357, 1632, 1601 cm^{-1}. HRMS calcd for $C_{22}H_{21}N_3NaO_2$: 382.1526, found: 382.1533.

Prepared according to general procedure A from this amine (1.600 g, 7.08 mmol) and 2-iodobenzoyl chloride (97%, 77.0.0 mg, 0.2800 mmol) the amide was obtained without further purification (162 mg, quantitative). ^{1}H NMR ($CDCl_3$, 300 MHz) major conformer δ 1.87 (br s, 1H), 3.38 (s, 3H), 3.44 (s, 3H), 6.85 (d, J=8.4 Hz, 2H), 6.98 (dd, J=7.2, 1.2 Hz, 2H), 7.14–7.19 (m, 5H), 7.24 (d, J=7.2 Hz, 1H), 7.30 (d, J=8.7 Hz, 1H), 7.40 (t, J=7.5 Hz, 1H), 7.48–7.52 (m, 3H), 7.90 (d, J=7.5 Hz, 1H), 8.40 (s, 1H). Minor conformer δ 3.33 (s, 3H), 7.63 (d, J=7.8 Hz, 2H), 7.69 (d, J=8.7 Hz, 1H), 7.84 (d, J=8.4 Hz, 1H), other signals masked by major conformer. Ratio 10:1. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 38.5 (CH_3), 38.6 (CH_3), 92.9 (Cq), 119.0 (CH), 126.2 (CH), 127.1 (CH), 127.2 (CH), 128.5 (CH), 128.7 (CH), 129.6 (CH), 130.0 (CH), 130.3 (CH), 131.3 (Cq), 131.7 (CH), 134.1 (Cq), 139.7 (Cq), 140.2 (CH), 142.2 (Cq), 144.7 (Cq), 146.2 (Cq), 167.7 (Cq), 169.9 (Cq), 170.0 (Cq). IR (film) 3257, 1632, 1596 cm^{-1}. HRMS calcd for $C_{29}H_{25}IN_3O_3$: 590.0935, found: 590.0929.

Prepared according to general procedure C from this amide (162 mg, 0.275 mmol) and iodomethane (0.2 mL, 3.21 mmol), after flash chromatography purification (DCM to DCM/MeOH 2%) the title compound was obtained (157 mg, 95%). Mp 138–140 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.97 (s, 3H), 3.49 (s, 3H), 3.52 (s, 3H), 6.72 (br s, 1H), 6.91–7.06 (m, 8H), 7.14 (br s, 1H), 7.11–7.18 (m, 2H), 7.21–7.31 (m, 4H), 7.70 (br d, J=8.1 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 37.4 (CH_3), 38.3 (CH_3), 38.7 (CH_3), 93.5 (Cq), 125.5 (CH), 126.0 (CH), 126.7 (CH), 126.8 (CH), 127.4 (CH), 128.5 (CH), 129.2 (CH), 129.5 (CH), 129.8 (CH), 130.1 (CH), 133.6 (Cq), 139.0 (Cq), 139.1 (CH), 141.8 (Cq), 144.3 (Cq), 144.6 (Cq), 145.4 (Cq), 169.1 (Cq), 169.3 (Cq), 169.8 (Cq). IR (film) 1643, 1603 cm^{-1}. HRMS calcd for $C_{30}H_{26}IN_3NaO_3$: 626.0911, found: 626.0924.

4.3.45. N-Methyl-N-(4-(N′-methyl-N′-(4-(N″-methyl-N″-phenyl)carbamoyl)phenyl)carbamoyl)phenyl-4-nitrobenzamide ***20a***. Prepared according to general procedure A from the amine derived from **19a** (750 mg, 2.09 mmol) and 4-nitrobenzoyl chloride (388 mg, 2.09 mmol) the amide was obtained without further purification (959 mg, 90%). Mp 228–230 °C. ^{1}H NMR ($CDCl_3$, 300 MHz) major conformer δ 3.40 (s, 3H), 3.44 (s, 3H), 6.82 (d, J=8.7 Hz, 2H), 6.97 (dd, J=7.2, 1.5 Hz, 2H), 7.14 (d, J=8.7 Hz, 2H), 7.15 (d, J=9.0 Hz, 2H), 7.16 (d, J=7.2 Hz, 1H), 7.24 (d, J=9.0 Hz, 2H), 7.45 (d, J=8.7 Hz, 2H), 8.05 (d, J=8.7 Hz, 2H), 8.30 (d, J=9.0 Hz, 2H), 8.51 (s, 1H). Minor conformer δ 3.33 (s, 3H), 3.38 (s, 3H), 6.75 (d, J=9.0 Hz, 2H), 6.90 (d, J=8.4 Hz, 2H), 7.38 (d, J=8.4 Hz, 2H), 7.98 (d, J=8.4 Hz, 2H), 8.24 (d, J=9.0 Hz, 2H), 8.44 (s, 1H), other signals masked by the major conformer. Ratio 10:1. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 38.2 (CH_3), 38.4

(CH_3), 119.1 (CH), 123.9 (CH), 125.9 (CH), 126.8 (CH), 128.5 (CH), 129.3 (CH), 129.7 (CH), 129.9 (CH), 131.5 (Cq), 133.8 (Cq), 139.1 (Cq), 140.3 (Cq), 144.5 (Cq), 145.8 (Cq), 149.8 (Cq), 163.8 (Cq), 169.6 (Cq), 169.8 (Cq). IR (film) 3368, 1641, 1600 cm^{-1}. HRMS calcd for $C_{29}H_{24}N_4NaO_5$: 531.1639, found: 531.1639.

Prepared according to general procedure C from this amide (268 mg, 0.527 mmol) and iodomethane (0.4 mL, 6.42 mmol) after flash chromatography purification (DCM to DCM/MeOH 6%) the title compound was obtained (266 mg, 97%). ^1H NMR ($CDCl_3$, 300 MHz) major conformer δ 3.40 (s, 3H), 3.47 (s, 3H), 3.53 (s, 3H), 6.76 (d, J=8.7 Hz, 2H), 6.82 (d, J=8.7 Hz, 2H), 7.04 (dd, J=8.1, 1.5 Hz, 2H), 7.09–7.26 (m, 2H), 7.13 (t, J=8.7 Hz, 4H), 7.22 (d, J=7.5 Hz, 1H), 7.35 (d, J=9.0 Hz, 2H), 8.03 (d, J=9.0 Hz, 2H), minor conformer δ 3.33 (s, 3H), 5.26 (s, 2H), 6.70 (d, J=8.4 Hz, 1H), 6.97 (d, J=7.5 Hz, 2H), 7.96 (d, J=8.7 Hz, 1H), 8.24 (d, J=9.0 Hz, 1H), 8.32 (d, J=9.0 Hz, 1H), other signals masked by major conformer. Ratio: 10:1. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 38.3 (CH_3), 38.4 (CH_3), 38.7 (CH_3), 123.4 (CH), 126.2 (CH), 126.4 (CH), 127.0 (CH), 127.2 (CH), 129.5 (CH), 129.87 (CH), 129.93 (CH), 130.3 (CH), 134.5 (Cq), 134.8 (Cq), 141.8 (Cq), 144.9 (Cq), 145.2 (Cq), 145.6 (Cq), 148.4 (Cq), 168.4 (Cq), 169.2 (Cq), 169.6 (Cq). IR (film) 1678, 1601, 1522, 1366, 1348 cm^{-1}. HRMS calcd for $C_{30}H_{27}N_4O_5$: 523.1976, found: 523.1974.

4.3.46. 2-Iodo-N-methyl-N-(4-(N′-methyl-N′-(4-(N″-methyl-N″-(4-(N‴-methyl-N‴-phenyl)carbamoyl)phenyl)carbamoyl)phenyl)carbamoyl)phenylbenzamide ***21a′***. Prepared according to general procedure B from **20a** (847 mg, 1.62 mmol) the amine was obtained without further purification (702 mg, 88%). ^1H NMR ($CDCl_3$, 300 MHz) δ 3.40 (s, 3H), 3.31 (s, 3H), 3.36 (s, 3H), 4.28 (br s, 2H), 6.29 (d, J=8.7 Hz, 2H), 6.73 (d, J=8.7 Hz, 2H), 6.76 (d, J=8.7 Hz, 2H), 6.87 (dd, J=7.5, 1.2 Hz, 2H), 6.93 (d, J=8.7 Hz, 2H), 7.01 (d, J=8.7 Hz, 2H), 7.10–7.14 (m, 5H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 37.66 (CH_3), 37.79 (CH_3), 37.82 (CH_3), 112.9 (CH), 125.3 (CH), 125.4 (CH), 126.4 (CH), 126.47 (Cq), 126.52 (CH), 128.8 (CH), 129.1 (CH), 129.4 (CH), 130.8 (CH), 132.4 (Cq), 133.2 (Cq), 144.2 (Cq), 145.3 (Cq), 146.7 (Cq), 148.9 (Cq), 169.2 (Cq), 169.3 (Cq), 170.0 (Cq). IR (film) 3351, 1634, 1602 cm^{-1}. HRMS calcd for $C_{30}H_{29}N_4O_3$: 493.2234, found: 493.2229.

Prepared according to general procedure A from this amine (50.0 mg, 0.101 mmol) and 2-iodobenzoyl chloride (97%, 30.0 mg, 0.109 mmol) after flash chromatography purification (DCM to DCM/MeOH 4%) the amide was obtained (66 mg, 90%). ^1H NMR ($CDCl_3$, 300 MHz) major conformer δ 2.93 (s, 3H), 3.33 (s, 3H), 3.46 (s, 3H), 6.76 (d, J=8.4 Hz, 2H), 6.85 (d, J=8.7 Hz, 2H), 6.92 (dd, J=8.1, 1.5 Hz, 2H), 7.08–7.23 (m, 10H), 7.46 (ddd, J=7.5, 7.2, 0.9 Hz, 1H), 7.56 (d, J=7.5 Hz, 2H), 7.60 (dd, J=7.5, 15 Hz, 1H), 7.96 (dd, J=8.1, 0.9 Hz, 1H), 9.66 (s, 1H). Minor conformer δ 3.41 (s, 3H), 7.89 (dd, J=7.8, 0.9 Hz, 1H), other signals masked by major conformer. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 37.8 (CH_3), 37.9 (CH_3), 38.0 (CH_3), 92.8 (Cq), 118.7 (CH), 125.8 (CH), 126.1 (CH), 126.7 (CH), 127.0 (CH), 128.0 (CH), 128.5 (CH), 128.9 (CH), 129.2 (CH), 129.5 (CH), 129.9 (Cq), 130.1 (CH), 130.9 (CH), 133.6 (Cq), 133.8 (Cq), 139.6 (CH), 140.1 (Cq), 142.7 (Cq), 143.9 (Cq), 145.6 (Cq), 146.2 (Cq), 168.2 (Cq), 169.6 (Cq), 170.0 (Cq), 170.6 (Cq). IR (film) 3256, 1642, 1632, 1601 cm^{-1}. HRMS calcd for $C_{37}H_{31}IN_4NaO_4$: 745.1282, found: 745.1293.

Prepared according to general procedure C from this amide (66.0 mg, 0.091 mmol) and iodomethane (0.1 mL, 1.60 mmol), after flash chromatography purification (DCM to DCM/MeOH 2%) the title compound was obtained (58 mg, 86%). ^1H NMR ($CDCl_3$, 300 MHz) δ 3.40 (s, 3H), 3.42 (s, 3H), 3.45 (s, 3H), 3.48 (s, 3H), 6.62 (br d, J=7.8 Hz, 1H), 6.78 (d, J=8.4 Hz, 2H), 6.85–7.02 (m, 9H), 7.11–7.23 (m, 8H), 7.63 (br d, J=7.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 37.4 (CH_3), 38.3 (CH_3), 38.5 (CH_3), 38.8 (CH_3), 93.8 (Cq), 125.8 (CH), 126.0 (CH), 126.4 (CH), 127.0 (CH), 127.1 (Cq), 127.2 (CH), 127.8 (CH), 128.9 (CH), 129.5 (CH), 129.9 (CH), 130.1 (CH), 130.2 (CH), 130.4 (CH), 133.1 (Cq), 133.9 (Cq), 134.3 (Cq), 139.4 (CH), 142.2 (Cq), 144.9 (Cq), 145.9 (Cq), 169.3 (Cq), 169.5 (Cq), 16.7 (Cq), 175.5 (Cq). IR (film) 1643, 1603 cm^{-1}. HRMS calcd for $C_{38}H_{33}IN_4NaO_4$: 759.1439, found: 759.1439.

4.3.47. N-Methyl-N-(4-(N′-methyl-N′-(4-(N″-methyl-N″-(4-(N‴-methyl-N‴-phenyl)carbamoyl)phenyl)carbamoyl)phenyl)carbamoyl)phenyl-4-nitrobenzamide ***21a***. Prepared according to general procedure A from the amine derived from **20a** (689 mg, 1.40 mmol) and 4-nitrobenzoyl chloride (282 mg, 1.52 mmol) after flash chromatography purification (DCM to DCM/MeOH 4%) the amide was obtained (813 mg, 90%). ^1H NMR ($CDCl_3$, 300 MHz) major conformer δ 3.36 (s, 6H), 3.48 (s, 3H), 6.82 (d, J=8.4 Hz, 2H), 6.86 (d, J=8.7 Hz, 2H), 6.99 (d, J=7.5 Hz, 2H), 7.09–7.15 (m, 6H), 7.25–7.30 (m, 4H), 7.55 (d, J=8.7 Hz, 2H), 8.32–8.34 (m, 3H), 10.16 (s, 1H). Minor conformer δ 3.30 (s, 3H), 3.44 (s, 3H), 7.48 (d, J=8.7 Hz, 1H), 8.05 (d, J=9.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 37.7 (CH_3), 37.8 (CH_3), 38.5 (CH_3), 118.9 (CH), 123.1 (CH), 125.9 (CH), 126.1 (CH), 126.5 (CH), 126.9 (CH), 128.7 (CH), 128.9 (CH), 129.1 (CH), 129.4 (CH), 129.7 (CH), 130.1 (Cq), 133.1 (Cq), 133.9 (Cq), 139.9 (Cq), 140.3 (Cq), 143.7 (Cq), 145.4 (Cq), 145.7 (Cq), 149.2 (Cq), 164.1 (Cq), 169.1 (Cq), 169.6 (Cq), 169.9 (Cq). IR (film) 3329, 1642, 1601, 1526, 1368, 1348 cm^{-1}. HRMS calcd for $C_{37}H_{32}N_5O_6$: 642.2347, found: 642.2354.

Prepared according to general procedure C from this amide (813 mg, 1.27 mmol) and iodomethane (0.8 mL, 12.8 mmol) after flash chromatography purification (DCM to DCM/MeOH 2%) the title compound was obtained (731 mg, 88%). ^1H NMR ($CDCl_3$, 300 MHz) major conformer δ 3.42 (s, 3H), 3.44 (s, 3H), 3.47 (s, 3H), 3.49 (s, 3H), 6.72 (d, J=8.4 Hz, 2H), 6.81 (d, J=8.4 Hz, 2H), 6.86 (d, J=8.4 Hz, 2H), 6.99 (dd, J=7.5, 1.8 Hz, 2H), 7.03 (d, J=8.7 Hz, 2H), 7.11 (d, J=8.7 Hz, 2H), 7.15 (d, J=8.4 Hz, 2H), 7.16–7.19 (m, 1H), 7.21 (d, J=7.5 Hz, 2H), 7.35 (d, J=9.0 Hz, 2H), 8.00 (d, J=9.0 Hz, 2H). Minor conformer δ 3.38 (s, 3H), 3.39 (s, 3H), 5.26 (s, 2H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 37.97 (CH_3), 38.07 (CH_3), 38.12 (CH_3), 38.4 (CH_3), 123.0 (CH), 125.82 (CH), 125.85 (CH), 126.2 (CH), 126.6 (CH), 126.8 (CH), 129.1 (CH), 129.50 (CH), 129.54 (CH), 129.7 (CH), 130.0 (CH), 133.8 (Cq), 133.9 (Cq), 134.2 (Cq), 141.5 (Cq), 144.6 (Cq), 145.0 (Cq), 145.4 (Cq), 145.5 (Cq), 147.9 (Cq), 168.0 (Cq), 168.9 (Cq), 169.0 (Cq), 169.3 (Cq). IR (film) 1645, 1602, 1521, 1367 cm^{-1}. HRMS calcd for $C_{38}H_{34}N_6O_5$: 656.2504, found: 656.2511.

4.3.48. N-Benzyl-4-nitro-N-phenylbenzamide ***18b***. Prepared according to general procedure A from 4-nitrobenzoyl chloride (5.09 g, 27.4 mmol), pyridine (7.5 mL, 92.8 mmol) and *N*-benzylaniline (5.02 g, 27.4 mmol), the title compound was obtained without further purification (9.04 g, 99%). ^1H NMR ($CDCl_3$, 300 MHz) δ 3.17 (s, 2H), 6.91–6.94 (m, 2H), 7.18–7.21 (m, 3H), 7.31–7.35 (m, 5H), 7.51 (d, J=8.7 Hz, 2H), 8.05 (d, J=8.7 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 54.2 (CH_2), 123.3 (CH), 127.8 (CH), 128.0 (CH), 128.2 (CH), 128.9 (CH), 129.7 (CH), 129.8 (CH), 137.1 (Cq), 142.5 (Cq), 142.6 (Cq), 148.2 (Cq), 168.6 (Cq). IR (film) 1647, 1522, 1400, 1390 cm^{-1}. HRMS calcd for $C_{20}H_{17}N_3O_2$: 333.1234, found: 333.1236. Anal. calcd for $C_{20}H_{16}N_2O_3$ (332.3): C, 72.28; H, 4.85; N, 8.43. Found: C, 72.03; H, 4.86; N, 8.40.

4.3.49. N-(4-(N′-Benzyl-N′-phenyl)carbamoyl)phenyl-2-iodo-N-methylbenzamide ***19b′***. Prepared according to general procedure B from **18b** (9.04 g, 27.2 mmol) the amine was obtained (7.5 g, 91%). ^1H NMR ($CDCl_3$, 300 MHz) major conformer δ 4.10 (br s, 2H), 5.16 (s, 2H), 6.41 (d, J=8.7 Hz, 2H), 6.98 (dd, J=8.4, 1.5 Hz, 2H), 7.18 (d, J=7.5 Hz, 2H), 7.22 (d, J=8.7 Hz, 2H), 7.09–7.38 (m, 6H). Minor conformer δ 5.09 (s, 2H), 6.34 (dd, J=8.7, 1.5 Hz, 2H), 6.92 (d, J=8.7 Hz, 2H). Ratio 20:1. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 54.4 (CH_2), 125.2 (CH), 126.5 (Cq), 127.5 (CH), 127.7 (CH), 128.5 (CH), 128.7 (CH), 129.3 (CH), 131.4 (CH), 138.2 (Cq), 144.8 (Cq), 148.6 (Cq), 170.8 (Cq). IR (film) 3358, 1632 cm^{-1}. HRMS calcd for $C_{20}H_{19}N_2O$: 303.1492, found: 303.1495.

Prepared according to general procedure A from this amine (100 mg, 0.331 mmol) and 2-iodobenzoyl chloride (97%, 83.0 mg,

0.302 mmol) the amide was obtained without further purification (176 mg, quantitative). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.07 (s, 2H), 6.94 (d, J=6.9 Hz, 2H), 7.05 (ddd, J=8.1, 7.2, 1.5 Hz, 1H), 7.14–7.35 (m, 12H), 7.45 (d, J=8.7 Hz, 2H), 7.81 (d, J=7.8 Hz, 1H), 8.70 (s, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 54.4 (CH_2), 92.2 (Cq), 119.2 (CH), 127.1 (CH), 127.7 (CH), 127.9 (CH), 128.3 (CH), 128.6 (CH), 128.8 (CH), 129.5 (CH), 130.2 (CH), 131.6 (CH), 137.7 (Cq), 139.7 (Cq), 140.2 (CH), 142.0 (Cq), 143.7 (Cq), 167.9 (Cq), 170.2 (Cq). IR (film) 3258, 1626, 1594 cm^{-1}. HRMS calcd for $C_{27}H_{22}IN_2O_2$: 533.0720, found: 533.0720.

Prepared according to general procedure C from this amide (175 mg, 0.329 mmol) and iodomethane (0.2 mL, 3.21 mmol), after flash chromatography purification (DCM to DCM/MeOH 2%) the title compound was obtained (163 mg, 91%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.43 (s, 3H), 5.09 (s, 2H), 6.76–6.98 (m, 6H), 7.07–7.18 (m, 5H), 7.23–7.32 (m, 6H), 7.61 (d, J=7.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 37.4 (CH_3), 54.0 (CH_2), 126.4 (CH), 127.1 (CH), 127.7 (CH), 127.9 (CH), 128.68 (CH), 128.73 (CH), 128.9 (Cq), 129.3 (CH), 129.7 (CH), 130.2 (CH), 134.7 (Cq), 137.5 (Cq), 139.4 (CH), 142.2 (Cq), 143.3 (Cq), 144.3 (Cq), 169.8 (Cq), 170.3 (Cq). IR (film) 1643 cm^{-1}. HRMS calcd for $C_{28}H_{23}IN_2NaO_2$: 569.0696, found: 569.0697.

4.3.50. N-(4-(N′-Benzyl-N′-phenyl)carbamoyl)phenyl-N-methyl-4-nitrobenzamide ***19b***. Prepared according to general procedure A from the amine derived from **18b** (8.80 g, 29.1 mmol) and 4-nitrobenzoyl chloride (5.40 g, 29.1 mmol) the amide was obtained without further purification (11.7 g, 89%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ major conformer 5.12 (s, 2H), 7.97 (dd, J=8.1, 1.5 Hz, 2H), 7.14–7.26 (m, 5H), 7.27–7.31 (m, 5H), 7.46 (d, J=8.7 Hz, 2H), 8.01 (d, J=9.0 Hz, 2H), 8.15 (d, J=9.0 Hz, 2H), 9.08 (s, 1H). Minor conformer δ 5.05 (s, 2H), 7.95 (d, J=8.4 Hz, 2H), 8.08 (d, J=9.0 Hz, 2H), other signals masked by the major conformer. Ratio 20:1. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 54.5 (CH_2), 119.9 (CH), 123.9 (CH), 127.3 (CH), 127.79 (CH), 127.82 (CH), 128.3 (CH), 128.8 (CH), 128.9 (CH), 129.5 (CH), 129.9 (CH), 132.0 (Cq), 137.4 (Cq), 139.5 (Cq), 140.5 (Cq), 143.5 (Cq), 149.8 (Cq), 164.3 (Cq), 170.6 (Cq). IR (film) 1623, 1595, 1527 cm^{-1}. HRMS calcd for $C_{27}H_{22}N_3O_4$: 452.1605, found: 452.1610. Anal. Calcd for $C_{27}H_{21}O_4N_3\cdot\frac{1}{4}H_2O$ (456.0): C, 71.83; H, 4.69; N, 9.31. Found: C, 70.87; H, 4.68; N, 9.20.

Prepared according to general procedure C from this amide (11.7 g, 25.9 mmol) and iodomethane (17 mL, 273 mmol) after flash chromatography purification (DCM to DCM/MeOH 10%) the title compound was obtained (6.23 g, 52%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.46 (s, 3H), 5.08 (s, 2H), 6.80–6.84 (m, 2H), 6.83 (d, J=8.4 Hz, 2H), 7.10–7.12 (m, 3H), 7.23 (d, J=8.1 Hz, 2H), 7.25–7.30 (m, 5H), 7.32 (d, J=8.7 Hz, 2H), 7.97 (d, J=8.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 38.2 (CH_3), 54.1 (CH_2), 123.3 (CH), 126.3 (CH), 127.2 (CH), 127.8 (CH), 128.2 (CH), 128.77 (CH), 128.79 (CH), 129.3 (CH), 129.7 (CH), 130.2 (CH), 135.3 (Cq), 137.3 (Cq), 141.9 (Cq), 143.2 (Cq), 144.9 (Cq), 148.1 (Cq), 168.4 (Cq), 169.5 (Cq). IR (film) 1647, 1521 cm^{-1}. HRMS calcd for $C_{28}H_{23}N_3O_4$: 488.1581, found: 488.1576.

4.3.51. 2-Iodo-N-methyl-N-(4-(N′-methyl-N′-(4-(N″-benzyl-N″-phenyl)carbamoyl)phenyl)carbamoyl)phenylbenzamide ***20b′***. Prepared according to general procedure B from **19b** (6.20 g, 13.3 mmol) the amine was obtained without further purification (5.8 g, quantitative). ^{1}H NMR ($CDCl_3$, 300 MHz) major conformer δ 3.38 (s, 3H), 3.91 (br s, 2H), 5.11 (s, 2H), 6.36 (d, J=8.4 Hz, 2H), 6.82 (d, J=8.7 Hz, 2H), 6.86–6.90 (m, 2H), 7.02 (d, J=8.7 Hz, 2H), 7.13–7.17 (m, 3H), 7.21 (d, J=8.4 Hz, 2H), 7.26–7.31 (m, 5H). Minor conformer δ 3.46 (s, 3H), 5.09 (s, 2H), 6.30 (d, J=8.7 Hz, 2H). Ratio 20:1. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 38.1 (CH_3), 53.8 (CH_2), 125.9 (CH), 127.0 (CH), 127.7 (CH), 127.9 (CH), 128.6 (CH), 128.7 (CH), 129.3 (CH), 130.0 (CH), 131.3 (CH), 133.4 (Cq), 137.6 (Cq), 143.6 (Cq), 147.1 (Cq), 148.2 (Cq), 148.3 (Cq), 169.6 (Cq), 170.4 (Cq). IR (film) 3352, 1632, 1600 cm^{-1}.

Prepared according to general procedure A from this amine (50.0 mg, 0.115 mmol) and 2-iodobenzoyl chloride (97%, 27.0 mg, 0.098 mmol) after flash chromatography purification (DCM to DCM/MeOH 4%) the amide was obtained (51 mg, 67%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.36 (s, 3H), 5.07 (s, 2H), 6.82–6.87 (m, 4H), 7.12–7.22 (m, 9H), 7.26–7.31 (m, 4H), 7.40 (ddd, J=7.5, 6.9, 1.2 Hz, 1H), 7.46–7.50 (m, 3H), 7.89 (d, J=7.8 Hz, 1H), 8.42 (s, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 38.5 (CH_3), 54.1 (CH_2), 92.8 (Cq), 119.0 (CH), 126.1 (CH), 127.4 (CH), 127.7 (CH), 127.9 (CH), 128.5 (CH), 128.7 (CH), 128.8 (CH), 129.5 (CH), 130.1 (CH), 130.3 (CH), 131.2 (Cq), 131.7 (CH), 134.1 (Cq), 137.5 (Cq), 139.7 (Cq), 140.3 (CH), 142.2 (Cq), 143.3 (Cq), 146.2 (Cq), 167.7 (Cq), 169.8 (Cq), 170.0 (Cq). IR (film) 3257, 1632, 1599 cm^{-1}. HRMS calcd for $C_{35}H_{29}IN_3O_3$: 666.1248, found: 666.1261.

Prepared according to general procedure C from this amide (51.0 mg, 0.077 mmol) and iodomethane (0.1 mL, 1.61 mmol), after flash chromatography purification (DCM to DCM/MeOH 2%) the title compound was obtained (47 mg, 90%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.36 (s, 3H), 3.45 (s, 3H), 5.12 (s, 2H), 6.66 (br d, J=7.2 Hz, 1H), 6.84–6.92 (m, 5H), 7.00 (br d, J=7.2 Hz, 2H), 8.11–7.20 (m, 6H), 7.27–7.32 (m, 7H), 7.53 (br d, J=7.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 37.0 (CH_3), 38.0 (CH_3), 54.0 (CH_2), 93.6 (Cq), 125.4 (CH), 126.0 (CH), 126.9 (CH), 127.5 (CH), 127.7 (CH), 128.47 (CH), 128.52 (CH), 129.1 (CH), 129.6 (CH), 129.8 (CH), 130.1 (CH), 133.60 (Cq), 133.62 (Cq), 137.1 (Cq), 139.2 (CH), 141.7 (Cq), 143.2 (Cq), 144.4 (Cq), 145.5 (Cq), 169.10 (Cq), 169.12 (Cq), 169.9 (Cq). IR (film) 1643, 1603 cm^{-1}. HRMS calcd for $C_{36}H_{31}IN_3O_3$: 680.1405, found: 680.1394.

4.3.52. N-Methyl-N-(4-(N′-methyl-N′-(4-(N″-benzyl-N″-phenyl)carbamoyl)phenyl)carbamoyl)phenyl-4-nitrobenzamide ***20b***. Prepared according to general procedure A from the amine derived from **19b** (1.10 g, 2.53 mmol) and 4-nitrobenzoyl chloride (470 mg, 2.53 mmol) followed by general procedure C using iodomethane (1.6 mL, 25.7 mmol) after flash chromatography purification (DCM to DCM/MeOH 4%) the title compound was obtained (1.25 g, 83%). ^{1}H NMR ($CDCl_3$, 500 MHz) major conformer δ 3.18 (s, 3H), 3.27 (s, 3H), 4.95 (s, 2H), 6.57 (d, J=8.5 Hz, 2H), 6.63 (d, J=8.5 Hz, 2H), 6.72 (d, J=7.0 Hz, 2H), 6.90–6.96 (m, 5H), 7.00 (d, J=8.5 Hz, 2H), 7.03–7.13 (m, 5H), 7.16 (d, J=8.5 Hz, 2H), 7.85 (d, J=9.0 Hz, 2H). Minor conformer δ 3.22 (s, 3H), 3.25 (s, 3H), 4.95 (s, 3H), 7.37 (d, J=8.5 Hz, 2H), 7.91 (d, J=9.0 Hz, 2H). Ratio 20:1. ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 38.3 (CH_3), 38.4 (CH_3), 54.2 (CH_2), 123.4 (CH), 126.1 (CH), 126.4 (CH), 127.1 (CH), 127.7 (CH), 128.1 (CH), 128.7 (CH), 128.8 (CH), 129.3 (CH), 129.8 (CH), 129.9 (CH), 130.3 (CH), 134.4 (Cq), 134.7 (Cq), 137.4 (Cq), 141.8 (Cq), 143.3 (Cq), 145.2 (Cq), 145.6 (Cq), 148.4 (Cq), 168.4 (Cq), 169.2 (Cq), 169.5 (Cq). IR (film) 1643, 1601, 1522, 1349 cm^{-1}. HRMS calcd for $C_{36}H_{30}N_4NaO_5$: 621.2108, found: 621.2108.

4.3.53. 2-Iodo-N-methyl-N-(4-(N′-methyl-N′-(4-(N″-methyl-N″-(4-(N‴-benzyl-N‴-phenyl)carbamoyl)phenyl)carbamoyl)phenyl)carbamoyl)phenylbenzamide ***21b′***. Prepared according to general procedure B from **20b** (1.20 g, 2.00 mmol) the amine was obtained without further purification (1.14 g, quantitative). ^{1}H NMR ($CDCl_3$, 300 MHz) major conformer δ 3.36 (s, 3H), 3.41 (s, 3H), 3.96 (br s, 2H), 5.09 (s, 2H), 6.25 (d, J=8.7 Hz, 2H), 6.74–6.83 (m, 6H), 6.98 (d, J=8.7 Hz, 2H), 7.06 (d, J=8.7 Hz, 2H), 7.11–7.14 (m, 3H), 7.18 (d, J=8.4 Hz, 2H), 7.28–7.31 (m, 5H). Minor conformer δ 3.30 (s, 3H), 3.40 (s, 3H), 6.58 (d, J=8.4 Hz, 2H), 7.51 (d, J=8.7 Hz, 2H), 7.71 (d, J=8.7 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 37.88 (CH_3), 37.91 (CH_3), 54.0 (CH_2), 113.0 (CH), 123.3 (Cq), 125.5 (CH), 125.6 (CH), 126.8 (CH), 127.4 (CH), 127.5 (CH), 128.3 (CH), 128.4 (CH), 128.9 (CH), 129.4 (CH), 129.6 (CH), 130.9 (CH), 132.9 (Cq), 133.8 (Cq), 137.4 (Cq), 143.6 (Cq), 146.1 (Cq), 147.4 (Cq), 149.2 (Cq), 169.7 (Cq), 169.8 (Cq), 170.6 (Cq). IR (film) 3352, 1642, 1632, 1599 cm^{-1}. HRMS calcd for $C_{36}H_{33}N_4O_3$: 569.2547, found: 569.2543.

Prepared according to general procedure A from this amine (300 mg, 0.528 mmol) and 2-iodobenzoyl chloride (97%, 123 mg,

0.448 mmol) the amide was obtained without further purification (421 mg, quantitative). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.28 (s, 3H), 3.44 (s, 3H), 4.52 (s, 2H), 6.31–6.76 (m, 4H), 6.82 (d, J=8.4 Hz, 2H), 6.96–6.99 (m, 2H), 7.01 (dd, J=7.8, 1.5 Hz, 2H), 7.07–7.14 (m, 7H), 7.18–7.24 (m, 4H), 7.32 (ddd, J=8.4, 7.5, 0.9 Hz, 1H), 7.49 (d, J=8.7 Hz, 2H), 7.54 (dd, J=7.5, 1.5 Hz, 1H), 7.82 (dd, J=8.1, 0.9 Hz, 1H), 9.69 (s, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 38.2 (CH_3), 38.3 (CH_3), 53.8 (CH_2), 93.1 (Cq), 119.1 (CH), 126.3 (CH), 127.5 (CH), 127.8 (CH), 128.1 (CH), 128.3 (CH), 128.6 (CH), 129.2 (CH), 129.3 (CH), 129.9 (CH), 130.1 (CH), 130.3 (CH), 131.3 (Cq), 133.6 (Cq), 134.1 (Cq), 136.7 (Cq), 139.9 (CH), 140.5 (Cq), 142.2 (Cq), 142.9 (Cq), 145.9 (Cq), 146.4 (Cq), 168.3 (Cq), 169.5 (Cq), 169.9 (Cq), 170.4 (Cq). IR (film) 3256, 1642, 1632, 1603 cm^{-1}. HRMS calcd for $C_{43}H_{36}IN_4O_4$: 799.1776, found: 799.1767.

Prepared according to general procedure C from this amide (435 mg, 0.544 mmol) and iodomethane (0.3 mL, 4.82 mmol), after flash chromatography purification (DCM to DCM/MeOH 3%) the title compound was obtained (47 mg, 79%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.31 (s, 3H), 3.33 (s, 3H), 5.37 (s, 3H), 5.02 (s, 2H), 6.54 (br d, J=7.8 Hz, 1H), 6.70 (d, J=8.4 Hz, 2H), 6.78–7.81 (m, 3H), 7.85–7.90 (m, 6H), 7.00–7.06 (m, 5H), 7.15–7.20 (m, 8H), 7.52 (br d, J=7.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 36.8 (CH_3), 37.6 (CH_3), 37.9 (CH_3), 53.6 (CH_2), 93.3 (Cq), 125.1 (CH), 125.4 (CH), 125.8 (CH), 126.5 (CH), 127.1 (CH), 127.4 (CH), 128.0 (CH), 128.1 (CH), 128.3 (CH), 128.7 (CH), 129.2 (CH), 129.4 (CH), 129.5 (CH), 129.8 (CH), 132.4 (Cq), 133.3 (Cq), 133.7 (Cq), 136.8 (Cq), 138.7 (CH), 141.6 (Cq), 142.8 (Cq), 144.1 (Cq), 145.3 (Cq), 169.2 (Cq), 169.3 (Cq), 169.5 (Cq), 170.0 (Cq). IR (film) 1642, 1603 cm^{-1}. HRMS calcd for $C_{44}H_{38}IN_4O_4$: 813.1932, found: 813.1945.

4.3.54. N-Methyl-N-(4-(N′-methyl-N′-(4-(N″-methyl-N″-(4-(N‴-benzyl-N‴-phenyl)carbamoyl)phenyl)carbamoyl)phenyl)carbamoyl) phenyl-4-nitrobenzamide ***21b***. To a solution of **S5** (see below) (504 mg, 1.68 mmol) in dry DCM (7 mL) was added oxalyl chloride (0.18 mL, 2.06 mmol) followed by a drop of DMF. After the effervescence stop the solution was stirred at rt under nitrogen for 2 h. The solvent was removed to dryness under reduced pressure and the residue was redissolved in DCM (10 mL). The amide derived from **19b** (366 mL, 0.84 mmol) and pyridine (0.50 mL, 6.18 mmol) were added and the mixture was stirred at rt overnight. The solution was partitioned between DCM and $NaHCO_3$ aqueous saturated solution and the organic phase was washed with $NaHCO_3$ aqueous saturated solution and HCl 3 N, and then it was dried, filtered and the solvent was removed under reduced pressure. The residue was redissolved in THF (30 mL) and iodomethane (0.6 mL, 9.64 mmol) following method C after flash chromatography purification (DCM to DCM/MeOH 5%) the title compound was obtained (256 mg, 42%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.43 (s, 3H), 3.49 (s, 3H), 3.48 (s, 3H), 5.12 (s, 2H), 6.72 (d, J=8.4 Hz, 1H), 6.80–6.89 (m, 6H), 7.04 (d, J=8.7 Hz, 1H), 7.10–7.22 (m, 8H), 7.21 (d, J=8.4 Hz, 1H), 7.28–7.34 (m, 7H), 7.35 (d, J=8.7 Hz, 1H), 7.99 (d, J=9.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 38.0 (CH_3), 38.1 (CH_3), 38.2 (CH_3), 54.0 (CH_2), 123.0 (CH), 125.8 (CH), 125.9 (CH), 126.2 (CH), 127.4 (CH), 127.6 (CH), 128.3 (CH), 128.41 (CH), 128.44 (CH), 129.0 (CH), 129.5 (CH), 129.8 (CH), 129.9 (CH), 130.9 (CH), 133.8 (Cq), 134.0 (Cq), 134.2 (Cq), 137.1 (Cq), 141.6 (Cq), 143.2 (Cq), 145.0 (Cq), 145.4 (Cq), 145.5 (Cq), 147.9 (Cq), 168.0 (Cq), 168.9 (Cq), 169.0 (Cq), 169.0 (Cq). IR (film) 1644, 1602 cm^{-1}. HRMS calcd for $C_{44}H_{38}N_5O_6$: 732.2817, found: 732.2815.

4.3.55. 2-Iodo-N-methyl-N-(4-(N′-methyl-N′-(4-(N″-methyl-N″-(4-(N‴-methyl-N‴-(4-(N⁗-benzyl-N⁗-phenyl)carbamoyl)phenyl)carbamoyl)phenyl)carbamoyl)phenyl)carbamoyl)phenylbenzamide ***22b′***. Prepared according to general procedure B from **21b** (262 mg, 0.358 mmol) the amine was obtained without further purification (227 mg, 90%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.40 (s, 3H), 3.42 (s, 3H), 3.43 (s, 3H), 4.16 (br s, 2H), 5.11 (s, 2H), 6.32 (d, J=8.7 Hz, 1H), 6.70 (d, J=8.4 Hz, 1H), 6.72 (d, J=8.7 Hz, 1H), 6.82 (d, J=8.7 Hz, 2H), 6.86–6.89 (m, 2H), 6.97 (d, J=8.7 Hz, 2H), 7.05 (d, J=8.7 Hz, 2H), 7.07 (d, J=8.7 Hz, 2H), 7.19 (d, J=8.7 Hz, 1H), 7.12–7.31 (m, 12H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 37.8 (CH_3), 38.0 (CH_3), 38.2 (CH_3), 53.9 (CH_2), 113.2 (CH), 123.6 (Cq), 125.6 (CH), 126.8 (CH), 127.4 (CH), 127.6 (CH), 128.29 (CH), 128.33 (CH), 128.4 (CH), 128.9 (CH), 129.0 (CH), 129.4 (CH), 129.6 (CH), 129.8 (CH), 131.0 (CH), 132.5 (Cq), 132.6 (Cq), 134.0 (Cq), 137.0 (Cq), 143.0 (Cq), 145.5 (Cq), 145.8 (Cq), 147.1 (Cq), 148.7 (Cq), 169.0 (Cq), 169.2 (Cq), 169.6 (Cq), 170.1 (Cq). IR (film) 3351, 1641, 1602 cm^{-1}. HRMS calcd for $C_{44}H_{39}N_5NaO_4$: 724.2894, found: 724.2887.

Prepared according to general procedure A from this amine (93.0 mg, 0.132 mmol) and 2-iodobenzoyl chloride (97%, 40.0 mg, 0.146 mmol) after flash chromatography purification (DCM to DCM/MeOH 2%) the amide was obtained (113 mg, 91%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.38 (s, 6H), 3.47 (s, 6H), 5.10 (s, 2H), 6.70 (d, J=8.4 Hz, 2H), 6.74 (d, J=8.4 Hz, 2H), 6.85–6.90 (m, 6H), 7.01 (d, J=8.4 Hz, 2H), 7.11–7.31 (m, 10H), 7.42 (d, J=7.5 Hz, 1H), 7.45 (d, J=8.1 Hz, 1H), 7.52 (d, J=8.7 Hz, 1H), 7.60 (dd, J=7.5, 1.5 Hz, 1H), 7.92 (d, J=7.8 Hz, 1H), 9.48 (s, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 37.8 (CH_3), 38.0 (CH_3), 38.1 (CH_3), 53.4 (CH_2), 92.8 (Cq), 118.7 (CH), 125.7 (CH), 125.9 (CH), 126.1 (CH), 126.9 (CH), 127.5 (CH), 127.7 (CH), 128.0 (CH), 128.38 (CH), 128.42 (CH), 128.46 (CH), 128.50 (CH), 128.9 (CH), 129.0 (CH), 129.7 (CH), 129.9 (CH), 130.1 (CH), 131.0 (Cq), 132.4 (Cq), 133.8 (Cq), 134.39 (Cq), 134.40 (Cq), 137.0 (Cq), 139.7 (CH), 140.0 (Cq), 143.1 (Cq), 145.0 (Cq), 145.9 (Cq), 146.3 (Cq), 167.8 (Cq), 162.2 (Cq), 169.3 (Cq), 170.2 (Cq). IR (film) 1642, 1633, 1602 cm^{-1}. HRMS calcd for $C_{51}H_{43}IN_5O_5$: 932.2303, found: 932.2291.

Prepared according to general procedure C from this amide (113 mg, 0.121 mmol) and iodomethane (0.2 mL, 3.21 mmol), after flash chromatography purification (DCM to DCM/MeOH 4%) the title compound was obtained (70 mg, 61%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.23 (s, 6H), 3.37 (s, 6H), 4.96 (s, 2H), 6.55 (br d, J=7.0 Hz, 1H), 6.60 (d, J=8.5 Hz, 2H), 6.62 (d, J=8.5 Hz, 2H), 6.69 (d, J=7.0 Hz, 2H), 6.78–6.80 (m, 4H), 6.87 (d, J=7.0 Hz, 4H), 6.94–6.97 (m, 6H), 7.03 (d, J=8.5 Hz, 2H), 7.09–7.13 (m, 6H), 7.47 (br d, J=7.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 37.0 (CH_3), 37.1 (CH_3), 38.0 (CH_3), 38.2 (CH_3), 53.9 (CH_2), 94.0 (Cq), 125.70 (CH), 125.72 (CH), 126.1 (CH), 126.8 (CH), 127.4 (CH), 127.6 (CH), 128.3 (CH), 128.4 (CH), 129.0 (CH), 129.5 (CH), 129.7 (CH), 129.8 (CH), 130.0 (CH), 132.9 (Cq), 133.4 (Cq), 133.7 (Cq), 134.0 (Cq), 137.0 (Cq), 139.1 (CH), 141.9 (Cq), 143.1 (Cq), 144.4 (Cq), 145.5 (Cq), 145.7 (Cq), 145.8 (Cq), 169.1 (Cq), 169.82 (Cq), 169.83 (Cq). IR (film) 1642, 1603 cm^{-1}. HRMS calcd for $C_{52}H_{45}IN_5O_5$: 946.2460, found: 946.2480.

4.3.56. N-Benzyl-4-nitro-N-phenyl-1-naphthamide ***24***. Prepared according to general procedure C from 4-nitro-1-naphthoic acid (1.00 g, 4.61 mmol), thionyl chloride (10 mL), pyridine (1.3 mL, 16.1 mmol) and *N*-phenylbenzamine (857 mg, 4.68 mmol). The crude product was purified by flash chromatography (Petrol to petrol/AcOEt 40%) to yield **24** (1.6 g, 90%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.25 (s, 2H), 6.34–6.80 (m, 2H), 7.00–6.97 (m, 3H), 7.26 (d, J=7.8 Hz, 1H), 7.41–7.33 (m, 5H), 7.67 (dd, J=7.2, 1.5 Hz, 1H), 7.69 (dd, J=7.2, 1.5 Hz, 1H), 7.91 (d, J=7.8 Hz, 1H), 8.22–8.18 (m, 1H), 8.46–8.43 (m, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 53.2 (CH_2), 122.4 (CH), 123.2 (CH), 123.4 (CH), 125.0 (Cq), 125.9 (CH), 127.6 (CH), 127.7 (CH), 127.8 (CH), 128.1 (CH), 128.6 (CH), 128.8 (CH), 129.0 (CH), 129.4 (CH), 131.2 (Cq), 136.8 (Cq), 140.6 (Cq), 141.3 (Cq), 146.3 (Cq), 168.4 (Cq), IR (film) 1651 cm^{-1} HRMS calcd for $C_{24}H_{19}N_2O_3$: 383.1390, found 383.1395.

4.3.57. N-(4-(N′-Benzyl-N′-phenyl)carbamoyl)-1-naphthyl-N-methyl-4-nitronaphthamide ***25a***. Prepared according to general procedure B from **24** (1.60 g, 4.19 mmol) the amine was obtained without further purification (1.23 g, 83%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.19 (br s, 2H), 5.23 (s, 2H), 6.34 (d, J=7.8 Hz, 1H), 6.88 (d, J=8.1 Hz, 2H), 6.93–6.97 (m, 3H), 7.02 (d, J=7.8 Hz, 1H), 7.26–7.41 (m, 6H), 7.51 (ddd, J=8.1 Hz, 7.2, 1.5, 1H), 7.67 (d, J=8.1 Hz,

1H), 8.22 (d, J=8.4 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 53.2 (CH_2), 107.4 (CH), 120.9 (CH), 122.9 (Cq), 124.0 (Cq), 124.7 (CH), 125.8 (CH), 126.2 (CH), 126.6 (CH), 127.0 (CH), 127.2 (CH), 127.4 (CH), 128.3 (CH), 128.4 (CH), 128.5 (CH), 131.6 (Cq), 137.7 (Cq), 143.2 (Cq), 143.4 (Cq), 170.9 (Cq). IR (film) 1628 cm^{-1} HRMS calcd for $C_{24}H_{21}N_2O$: 353.1648, found 353.1655.

Prepared according to general procedure A from this amine (294 mg, 0.835 mmol) and 4-nitro-1-naphthoyl chloride (203 mg, 0.861 mmol) after flash chromatography purification (petrol to AcOEt) the amide was obtained (446 mg, 97%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.94 (s, 2H), 6.65–6.74 (m, 2H), 6.84–6.94 (m, 4H), 7.09–7.15 (m, 2H), 7.18–7.26 (m, 3H), 7.31 (dd, J=7.5, 7.0 Hz, 1H), 7.41 (dd, J=8.0, 7.0 Hz, 1H), 7.46 (d, J=7.0 Hz, 1H), 7.57 (d, J=7.5 Hz, 1H), 7.66 (dd, J=7.5, 7.0 Hz, 1H), 7.74 (dd, J=8.0, 7.0 Hz, 1H), 7.79 (d, J=7.5 Hz, 1H), 7.86 (d, J=8.5 Hz, 1H), 8.08 (d, J=8.0 Hz, 1H), 8.37 (d, J=7.5 Hz, 1H), 8.48 (d, J=9.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 53.6 (CH_2), 119.9 (CH), 122.0 (CH), 122.8 (CH), 123.6 (CH), 124.0 (CH), 125.6 (CH), 126.5 (CH), 127.0 (CH), 127.3 (CH), 127.7 (CH), 127.9 (CH), 128.5 (CH), 128.6 (CH), 128.8 (CH), 129.3 (CH), 129.8 (CH), 130.8 (Cq), 131.3 (Cq), 131.8 (Cq), 133.0 (Cq), 137.0 (Cq), 140.5 (Cq), 142.1 (Cq), 148.0 (Cq), 167.1 (Cq), 170.8 (Cq), IR (film) 3237, 1625 cm^{-1} HRMS calcd for $C_{35}H_{26}N_3O_2$: 552.1918, found 552.1909.

Prepared according to general procedure C from the amide (223 mg, 0.404 mmol) and methyl iodide (0.25 mL, 4.01 mmol), after flash chromatography purification (petrol to AcOEt) the title compound was obtained (231 mg, quantitative). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.50 (s, 3H), 4.98 (d, J=14.3 Hz, 1H), 5.10 (d, J=14.3 Hz, 1H), 6.44 (d, J=7.2 Hz, 2H), 6.59–6.63 (m, 2H), 6.67–6.70 (m, 2H), 6.75 (dd, J=7.2, 7.0 Hz, 1H), 6.83 (d, J=7.2 Hz, 1H), 7.22–7.18 (m, 5H), 7.48 (d, J=7.8 Hz, 1H), 7.52 (d, J=7.2 Hz, 1H), 7.55 (d, J=7.5 Hz, 1H), 7.58 (d, J=7.0 Hz, 1H), 7.61 (d, J=7.5 Hz, 1H), 7.91 (d, J=8.2 Hz, 1H), 7.99 (d, J=8.2 Hz, 1H), 8.15 (d, J=7.8 Hz, 1H), 8.37 (d, J=8.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 37.8 (CH_3), 52.8 (CH_2), 121.4 (CH), 122.2 (CH), 122.5 (CH), 123.1 (CH), 124.1 (CH), 124.77 (CH), 124.81 (Cq), 126.0 (CH), 126.2 (CH), 126.8 (CH), 127.2 (CH), 127.5 (CH), 127.6 (CH), 127.8 (CH), 128.0 (CH), 128.3 (CH), 128.4 (CH), 128.6 (CH), 129.2 (Cq), 129.3 (CH), 130.9 (Cq), 131.3 (Cq), 135.2 (Cq), 136.9 (Cq), 139.5 (Cq), 140.1 (Cq), 141.4 (Cq), 146.2 (Cq), 169.06 (Cq), 169.10 (Cq). IR (film) 1646 cm^{-1}. HRMS calcd for $C_{36}H_{28}N_3O_4$: 566.2074, found 566.2078.

4.3.58. N-Benzyl-N-(4-(N′-Benzyl-N′-phenyl)carbamoyl)-1-naphtyl-4-nitronaphtamide ***25b***. Prepared according to general procedure C from the same amide (221 mg, 0.401 mmol) and benzyl bromide (0.2 mL, 1.67 mmol), after flash chromatography purification (petrol to petrol/AcOEt 50%) the title compound was obtained (257 mg, quantitative). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.15 (d, J=14.0 Hz, 1H), 4.99 (d, J=14.0 Hz, 1H), 5.06 (d, J=14.0 Hz, 1H), 5.96 (d, J=14.0 Hz, 1H), 6.12–6.12 (m, 1H), 6.39–6.46 (m, 2H), 6.51 (d, J=7.5 Hz, 1H), 6.59–6.68 (m, 1H), 6.75–6.83 (m, 1H), 6.85–6.90 (m, 1H), 7.07–7.13 (m, 1H), 7.17–7.25 (m, 12H), 7.48 (d, J=8.0 Hz, 1H), 7.50 (d, J=7.5 Hz, 1H), 7.54 (d, J=7.0 Hz, 1H), 7.57 (d, J=7.0 Hz, 1H), 7.93–7.97 (m, 1H), 8.01 (d, J=9.0 Hz, 1H), 8.34 (d, J=8.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 52.5 (CH_2), 52.8 (CH_2), 121.0 (CH), 122.3 (CH), 122.4 (CH), 123.0 (CH), 124.4 (CH), 124.7 (Cq), 125.6 (CH), 126.0 (CH), 126.2 (CH), 126.7 (CH), 127.2 (CH), 127.4 (CH), 127.7 (CH), 127.9 (CH), 128.2 (CH), 128.4 (CH), 128.5 (CH), 129.2 (CH), 129.6 (CH), 130.9 (Cq), 131.3 (Cq), 135.0 (Cq), 136.4 (Cq), 136.8 (Cq), 136.9 (Cq), 140.0 (Cq), 141.5 (Cq), 146.1 (Cq), 168.8 (Cq), 169.1 (Cq). IR (film) 1646 cm^{-1}. HRMS calcd for $C_{42}H_{35}N_4O_4$: 659.2653, found 659.2644. (M+NH$_4$).

4.3.59. N-Methyl-N-(4-(N′-methyl-N′-(4-(N″-benzyl-N″-phenyl)carbamoyl)-1-naphtyl)carbamoyl)-1-naphtyl-4-nitronapthamide ***26a***. Prepared according to general procedure B from **25a** (231 mg, 0.409 mmol) the amine was obtained without further purification (219 mg, quantitative). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.52 (s, 3H), 4.19 (br s, 2H), 5.15 (d, J=14.0 Hz, 1H), 5.24 (d, J=14.0 Hz, 1H), 5.90 (d, J=7.8 Hz, 1H), 6.60 (d, J=7.2 Hz, 2H), 6.68 (d, J=7.8 Hz, 1H), 6.72–6.81 (m, 4H), 6.90 (d, J=7.2 Hz, 1H), 7.30–7.40 (m, 6H), 7.48 (dd, J=7.8, 7.2 Hz, 1H), 7.56–7.65 (m, 3H), 8.03 (d, J=7.5 Hz, 1H), 8.13 (d, J=7.5 Hz, 1H), 8.23 (d, J=8.4 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 37.6 (CH_3), 52.6 (CH_2), 107.1 (CH), 120.8 (CH), 122.6 (CH), 123.0 (CH), 123.4 (Cq), 123.7 (CH), 124.3 (CH), 125.1 (CH), 125.4 (CH), 125.7 (CH), 125.8 (CH), 126.3 (CH), 126.4 (CH), 126.9 (CH), 127.0 (CH), 127.1 (CH), 127.3 (CH), 128.3 (CH), 129.3 (Cq), 131.2 (Cq), 133.6 (Cq), 137.0 (Cq), 141.5 (Cq), 143.3 (Cq), 170.0 (Cq), 172.5 (Cq). IR (film) 1632 cm^{-1}. HRMS calcd for $C_{36}H_{30}N_3O_2$: 536.2333, found: 536.2336.

Prepared according to general procedure A from this amine (233 mg, 0.435 mmol) and 4-nitro-1-naphthoyl chloride (118 mg, 0.501 mmol) the amide was obtained without further purification (127 mg, 40%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.33 (s, 3H), 5.01 (s, 2H), 6.43–6.53 (m, 2H), 6.61–6.85 (m, 5H), 6.91–7.05 (m, 1H), 7.14–7.29 (m, 7H), 7.38 (d, J=7.8 Hz, 1H), 7.40 (d, J=7.2 Hz, 1H), 7.48 (d, J=7.2 Hz, 1H), 7.53 (d, J=7.2 Hz, 1H), 7.61–7.70 (m, 4H), 7.75–7.89 (m, 2H), 7.94 (d, J=8.4 Hz, 1H), 8.16 (d, J=8.4 Hz, 1H), 8.39 (d, J=8.4 Hz, 1H), 9.46 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 37.4 (CH_3), 52.7 (CH_2), 119.3 (CH), 121.8 (CH), 122.1 (CH), 122.8 (CH), 122.9 (CH), 123.2 (CH), 123.3 (CH), 123.4 (CH), 123.8 (CH), 124.9 (CH), 125.1 (Cq), 125.6 (CH), 125.8 (CH), 126.1 (CH), 126.2 (CH), 126.7 (CH), 126.8 (CH), 127.0 (CH), 127.5 (CH), 128.1 (CH), 128.4 (CH), 128.5 (CH), 129.3 (Cq), 129.4 (CH), 130.4 (Cq), 131.0 (Cq), 131.1 (Cq), 131.4 (Cq), 132.8 (Cq), 134.4 (Cq), 136.8 (Cq), 139.5 (Cq), 140.3 (Cq), 141.4 (Cq), 166.5 (Cq), 169.2 (Cq), 171.0 (Cq). IR (film) 3239, 1623 cm^{-1}. HRMS calcd for $C_{47}H_{34}N_4NaO_5$: 757.2421, found 757.2411.

Prepared according to general procedure C from this amide (127 mg, 0.173 mmol) and methyl iodide (0.2 mL, 3.21 mmol), after flash chromatography purification (DCM to DCM/MeOH 2%) the title compound was obtained (116 mg, 90%). ^{1}H NMR and ^{13}C NMR show mixture of multiple conformers. IR (film) 1644 cm^{-1}. HRMS calcd for $C_{48}H_{37}N_4NaO_5$: 749.2758, found: 749.2754.

4.3.60. N-Benzyl-N-(4-(N′-benzyl-N′-(4-(N″-benzyl-N″-phenyl)carbamoyl)-1-naphtyl)carbamoyl)-1-naphtyl-4-nitronapthamide ***26b***. Prepared according to general procedure B from **25b** (280 mg, 0.437 mmol) the amine was obtained without further purification (195 mg, 73%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.98 (br s, 2H), 4.27 (d, J=13.5 Hz, 1H), 5.18 (s, 2H), 6.94 (d, J=7.8 Hz, 1H), 6.03 (d, J=13.5 Hz, 1H), 6.27 (d, J=7.5 Hz, 1H), 6.60–6.65 (m, 3H), 6.74 (d, J=7.8 Hz, 1H), 6.79.6.88 (m, 2H), 6.99 (dd, J=7.5, 7.2 Hz, 1H), 7.12–7.40 (m, 11H), 7.45 (dd, J=7.8, 7.5 Hz, 1H), 7.57–7.64 (m, 3H), 8.10 (d, J=8.1 Hz, 1H), 8.05–8.17 (m, 2H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 52.4 (CH_2), 52.7 (CH_2), 107.3 (CH), 120.8 (CH), 122.7 (Cq), 123.0 (CH), 123.8 (Cq), 124.4 (CH), 124.8 (CH), 124.9 (CH), 125.6 (CH), 125.8 (CH), 125.9 (CH), 126.4 (CH), 126.5 (CH), 127.0 (CH), 127.2 (CH), 127.4 (CH), 128.0 (CH), 128.2 (CH), 128.4 (CH), 129.5 (CH), 131.2 (Cq), 133.7 (Cq), 137.1 (Cq), 137.2 (Cq), 138.7 (Cq), 141.8 (Cq), 143.1 (Cq), 170.0 (Cq), 171.9 (Cq). IR (film) 1633 cm^{-1}. HRMS calcd for $C_{42}H_{34}N_3O_2$: 612.2646, found: 612.2647.

Prepared according to general procedure A from this amine (195 mg, 0.319 mmol) and 4-nitro-1-naphthoyl chloride (86.0 mg, 0.365 mmol) the amide was obtained without further purification (258 mg, quantitative). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.10 (d, J=13.2 Hz, 1H), 4.99 (br s, 2H), 5.83 (d, J=13.2 Hz, 1H), 6.14 (d, J=7.2 Hz, 1H), 6.31 (d, J=6.9 Hz, 1H), 6.52 (d, J=6.9 Hz, 2H), 6.63 (d, J=8.1 Hz, 1H), 6.75 (d, J=7.2 Hz, 1H), 6.84–7.07 (m, 7H), 7.12–7.33 (m, 7H), 7.38 (d, J=7.8 Hz, 1H), 7.41 (d, J=7.2 Hz, 1H), 7.46 (d, J=7.2 Hz, 1H), 7.49 (d, J=7.5 Hz, 1H), 7.60–7.69 (m, 4H), 7.86 (d, J=9.0 Hz, 1H), 7.90 (d, J=9.0 Hz, 1H), 7.98 (d, J=8.1 Hz, 1H), 8.10 (d, J=8.4 Hz, 1H), 8.36 (d, J=8.4 Hz, 1H), 9.44 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 52.7 (CH_2), 52.4 (CH_2), 119.9 (CH), 122.0 (CH), 122.1 (CH), 122.8 (CH), 123.3 (CH), 124.6 (Cq), 124.8 (CH), 125.3 (CH), 125.8 (CH), 125.9 (CH), 126.0 (CH), 126.2 (CH), 126.7 (CH), 126.8 (CH), 127.2 (CH), 127.4 (CH), 127.5 (CH), 127.8 (CH), 128.1 (CH), 128.3 (CH), 128.4 (CH), 129.2 (Cq), 129.3 (CH), 129.5 (CH), 130.5 (Cq), 131.0 (Cq), 131.1

(Cq), 131.7 (Cq), 132.8 (Cq), 134.3 (Cq), 136.5 (Cq), 136.7 (Cq), 137.5 (Cq), 139.3 (Cq), 141.5 (Cq), 147.5 (Cq), 147.6 (Cq), 166.4 (Cq), 169.3 (Cq), 170.5 (Cq). IR (film) 3240, 1630 cm^{-1}. HRMS calcd for $C_{53}H_{42}N_5O_5$: 828.3180, found 828.3163.

Prepared according to general procedure C from this amide (257 mg, 0.310 mmol) and benzyl bromide (0.2 mL, 1.67 mmol), after flash chromatography purification (petrol to petrol/AcOEt 20%) the title compound was obtained (235 mg, 82%). ^1H NMR and ^{13}C NMR show a complex mixture of multiple conformers. IR (film) 1645 cm^{-1}. HRMS calcd for $C_{60}H_{44}N_4NaO_5$: 923.3204, found: 923.3215.

4.3.61. N-Methyl-N-(4-(N′-methyl-N′-(4-(N″-methyl-N″-(4-(N‴-benzyl-N‴-phenyl)carbamoyl)-1-naphtyl)carbamoyl)-1-naphtyl)carbamoyl)-1-naphtyl-4-nitronapthamide ***27a***. Prepared according to general procedure B from **26a** (116 mg, 0.159 mmol) the amine was obtained without further purification (111 mg, quantitative). ^1H NMR and ^{13}C NMR show a mixture of multiple conformers. IR (film) 1642, 1632 cm^{-1}. HRMS calcd for $C_{48}H_{39}N_4O_3$: 719.3032, found: 719.3017.

Prepared according to general procedure A from this amine (133 mg, 0.185 mmol) and 4-nitro-1-naphthoyl chloride (52.0 mg, 0.221 mmol) the amide was obtained without further purification (130 mg, 76%). ^1H NMR and ^{13}C NMR show mixture of multiple conformers. IR (film) 1641,1633 cm^{-1}. HRMS calcd for $C_{59}H_{43}N_5NaO_6$: 940.3106, found: 940.3108.

Prepared according to general procedure C from this amide (130 mg, 0.142 mmol) and methyl iodide (0.15 mL, 2.41 mmol), after flash chromatography purification (Petrol to AcOEt) the title compound was obtained (70 mg, 53%). ^1H NMR and ^{13}C NMR show mixture of multiple conformers. IR (film) 1643, 1588 cm^{-1}. HRMS calcd for $C_{60}H_{45}N_5NaO_6$: 954.3262, found: 954.3258.

4.3.62. N-Benzyl-N-(4-(N′-benzyl-N′-(4-(N″-benzyl-N″-(4-(N‴-benzyl-N‴-phenyl)carbamoyl)-1-naphtyl)carbamoyl)-1-naphtyl)carbamoyl)-1-naphtyl-4-nitronapthamide ***27b***. Prepared according to general procedure B from **26b** (235 mg, 0.261 mmol) the amine was obtained without further purification (227 mg, quantitative). ^1H NMR and ^{13}C NMR show mixture of multiple conformers. IR (film) 1642, 1632 cm^{-1}. HRMS calcd for $C_{60}H_{46}N_4NaO_3$: 893.3449, found: 893.3462.

Prepared according to general procedure A from this amine (240 mg, 0.276 mmol) and 4-nitro-1-naphthoyl chloride (77.0 mg, 0.327 mmol) the amide was obtained without further purification (248 mg, 84%). ^1H NMR and ^{13}C NMR show mixture of multiple conformers. IR (film) 1641,1630 cm^{-1}. MS (ESI^+) 1093 (M+Na, 50), 1124 (M+Na+MeOH, 100).

Prepared according to general procedure C from this amide (248 mg, 0.232 mmol) and benzyl bromide (0.15 mL, 1.25 mmol), after flash chromatography purification (petrol to AcOEt) the title compound was obtained (61 mg, 23%). ^1H NMR and ^{13}C NMR show mixture of multiple conformers. IR (film) 1647,1587 cm^{-1}. MS (ESI^+) 1182 (M+Na).

4.3.63. Methyl 4-(4-nitro-benzoylamino)benzoate ***S1***. Prepared according to general procedure A from methyl 4-aminobenzoate (1.25 g, 8.26 mmol) and 4-nitrobenzoyl chloride (2.02 g, 10.9 mmol) the title compound was obtained without further purification (2.33 g, 99%). ^1H NMR (DMSO-d_6, 300 MHz) δ 3.84 (s, 3H), 7.94 (d, J=9.0 Hz, 2H), 7.99 (d, J=9.0 Hz, 2H), 8.19 (dd, J=9.0, 1.8 Hz, 2H), 8.38 (dd, J=9.0, 1.8 Hz, 2H), 10.88 (s, 1H). ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ 52.7 (CH_3), 120.5 (CH), 124.3 (CH), 125.5 (Cq), 130.1 (CH), 130.9 (CH), 140.9 (Cq), 143.9 (Cq), 150.0 (Cq), 165.1 (Cq), 166.5 (Cq). IR (film) 3378, 1688 cm^{-1}. HRMS calcd for $C_{15}H_{11}N_2O_5$: 299.0673, found: 299.0671.

4.3.64. Methyl 4-(N-methyl-N-(4-nitro-benzoyl)amino)benzoate ***S2***. Prepared according to general procedure C from **S1** (995 mg, 3.32 mmol) and iodomethane (2.2 mL, 35.3 mmol) after flash chromatography purification (DCM to DCM/MeOH 2%) the title compound was obtained (658 mg, 63%). ^1H NMR ($CDCl_3$, 300 MHz) δ 3.57 (s, 3H), 3.90 (s, 3H), 7.11 (d, J=8.7 Hz, 2H), 7.47 (d, J=9.0 Hz, 2H), 7.94 (d, J=8.7 Hz, 2H), 8.06 (d, J=9.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 38.4 (CH_3), 52.6 (CH_3), 123.5 (CH), 126.8 (CH), 129.0 (Cq), 129.9 (CH), 131.2 (CH), 141.8 (Cq), 148.0 (Cq), 148.5 (Cq), 166.1 (Cq), 168.5 (Cq). IR (film) 1720, 1655, 1523 cm^{-1}. HRMS calcd for $C_{16}H_{14}N_5O_2$: 314.0897, found: 314.0899.

4.3.65. tert-Butyl 4-(4-nitro-benzoylamino)benzoate ***S3***. Prepared according to general procedure A from *tert*-butyl 4-aminobenzoate (1.04 g, 5.37 mmol) and 4-nitrobenzoyl chloride (960 mg, 5.17 mmol) the title compound was obtained without further purification (741 mg, 42%). ^1H NMR (DMSO-d_6, 300 MHz) δ 1.57 (s, 9H), 7.94 (s, 4H), 8.22 (d, J=9.0 Hz, 2H), 8.40 (d, J=9.0 Hz, 2H), 10.87 (s, 1H). ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ 28.5 (CH_3), 81.1 (Cq), 120.3 (CH), 124.3 (CH), 127.3 (Cq), 130.1 (CH), 130.7 (CH), 140.9 (Cq), 143.5 (Cq), 150.0 (Cq), 165.0 (Cq), 165.3 (Cq). IR (film) 3385, 1678, 1526, 1310, 1298 cm^{-1}. HRMS calcd for $C_{18}H_{18}N_2O_5$: 342.1210, found: 342.1213.

4.3.66. tert-Butyl 4-(N-methyl-N-(4-nitro-benzoyl)amino)benzoate ***S4***. Prepared according to general procedure C from **S3** (700 mg, 2.05 mmol) and iodomethane (4.27 mL, 68.6 mmol) after flash chromatography purification (DCM to DCM/MeOH 2%) the title compound was obtained (697 mg, 96%). ^1H NMR ($CDCl_3$, 300 MHz) δ 1.56 (s, 9H), 3.53 (s, 3H), 7.09 (d, J=8.7 Hz, 2H), 7.47 (d, J=9.0 Hz, 2H), 7.87 (d, J=8.7 Hz, 2H), 8.05 (d, J=9.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 28.3 (CH_3), 81.8 (Cq), 123.5 (CH), 126.6 (CH), 129.8 (CH), 131.0 (CH), 131.5 (Cq), 141.9 (Cq), 147.6 (Cq), 148.4 (Cq), 164.7 (Cq), 168.5 (Cq). IR (film) 1711, 1650, 1524, 1368, 1347 cm^{-1}. HRMS calcd for $C_{19}H_{21}N_2O_5$: 357.1445, found: 357.1452.

4.3.67. 4-(N-Methyl-N-(4-nitro-benzoyl)amino)benzoic acid ***S5***. To a solution of **S4** (103 mg, 0.289 mmol) in dry DCM (5 mL) at 0 °C TFA (1 mL) was added. The mixture was stirred at 0 °C for 2.5 h. The organics were removed under reduced pressure to yield **S5** (87 mg, quantitative). ^1H NMR ($CDCl_3$, 300 MHz) δ 3.59 (s, 3H), 7.19 (d, J=8.4 Hz, 2H), 7.47 (d, J=8.7 Hz, 2H), 8.01 (d, J=8.4 Hz, 2H), 8.08 (d, J=8.7 Hz, 2H), 8.37 (s, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 39.0 (CH_3), 123.9 (CH), 127.2 (CH), 128.3 (Cq), 129.8 (CH), 132.2 (CH), 140.2 (Cq), 148.1 (Cq), 148.9 (Cq), 170.6 (Cq), 170.9 (Cq).

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.06.037.

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