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Microwave-Assisted Synthesis of Naphthalenemonoimides and N-Desymmetrized Naphthalenediimides

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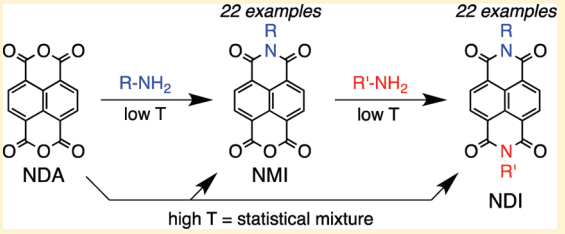
Supporting Information

ABSTRACT: Naphthalenemonoimides and N-desymmetrized naphthalenediimides were synthesized using a stepwise microwave-assisted protocol. The steric and electronic properties of aliphatic amines determined the outcome of the reactions, while in the amino acid series their ability to solubilize the naphthalene dianhydride starting material was crucial. Molecular modeling was used to rationalize the observed selectivity.



INTRODUCTION

We report herein the stepwise and high-yielding synthesis of naphthalenemonoimides (NMIs) and N-desymmetrized naphthalenediimides (NDIs). We also investigate the factors which influence the efficiency of this microwave-assisted process, such as the steric crowding at the α-carbon, the solubility of the amine reactant, and the noncovalent interaction between the reagents. The main benefits of this method are the straightforward synthesis and purification of NMIs, the ability to control the reactivity of naphthalene dianhydride (NDA), and the production of N-desymmetrized NDIs with a broad range of structural variety. Furthermore, the observed selectivity for the monofunctionalization of NDA was rationalized using molecular modeling at the ab initio level.

The NDIs represent a class of compounds with an electron-deficient π-system whose electronic and spectroscopic properties have led to their extensive study in the field of supramolecular chemistry.[1] As an electron-acceptor motif, their ability to form donor−acceptor interactions has been widely exploited in the construction of molecular devices and machines.[2] The electronic properties of the π-surface, however, may be altered by core substitution: the π-acidity of unsubstituted NDIs has facilitated the development of transmembrane anion transport systems,[3] while the attachment of electron-donating substituents at the naphthyl core can be employed in the synthesis of electrooptically active molecular materials.[4] Water-soluble NDI derivatives have been employed by the Iverson group as DNA intercalators,[5] while the Sanders group has used them as building blocks in dynamic combinatorial libraries, leading to the formation of a wide variety of catenanes.[6] Organic-soluble amino acid-functionalized NDI derivatives have been shown to spontaneously self-assemble into hydrogen-bonded helical nanotubes with a well-defined interior cavity capable of complexing various guests, including fullerenes, ion pairs, and polyaromatic hydrocarbons.[7]

Mild stepwise functionalization of NDA (**1**) using α-amino acids and microwave dielectric heating was previously reported by the Sanders group as an efficient one-pot method for the synthesis of NDIs. This method is particularly suitable for symmetrically substituted NDIs and has found limited application to N-desymmetrized derivatives.[8] The literature regarding efficient synthesis and isolation of NMIs **2**, however, is scant due to the difficulty involved in controlling the reaction of 1 equiv of an amine with a cross-conjugated molecule containing two equivalent electrophilic sites such as NDA.

RESULTS AND DISCUSSION

All reactions were run in a dedicated microwave reactor in pressure-resistant, tightly sealed tubes. The reactions were carried out in two stages, first a mild heating at 40 °C (amino acids and their derivatives) or 75 °C (alkylamines) for 5 min followed by heating for 5−15 min at 140 °C. The microwave maximum power input was set to 300 W, and the temperature was held at 75 °C by 5−20 W pulses. In the second step, the temperature was set to 140 °C and was maintained by pulses of 30−50 W. The synthesis of NMIs **2a**−**g** using alkylamines is outlined in Scheme 1 with the reaction conditions and yields reported in Table 1, entries 1−7.

The data from this study suggest that the steric bulk at the α-carbon influences significantly the outcome of the reaction: amines attached to a secondary carbon gave consistently higher yields than when connected to a tertiary carbon. Furthermore, amines with tertiary α-carbons required longer reaction times (up to 15 min at 140 °C) to force the condensation to completion. For 1-adamantanamine, where the nucleophile is attached to a quaternary carbon, the ^{1}H NMR spectrum of the product

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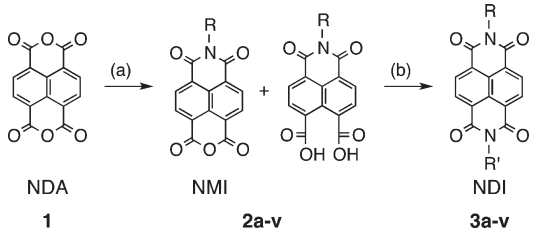
Scheme 1. General Protocol for the Microwave Synthesis of NMIs 2a−v and Desymmetric NDIs 3a−v[a]



[a] Reagents and conditions for alkylamines: (a) RNH_2, DMF, (i) 75 °C, 5 min, (ii) 140 °C, 5−15 min; (b) $R'NH_2$, DMF, (i) 75 °C, 5 min, (ii) 140 °C, 5−15 min. Reagents and conditions for amino acids: (a) RNH_2, Et_3N, DMF, (i) 40 °C, 5 min, (ii) 140 °C, 5 min; (b) $R'NH_2$, Et_3N, DMF, (i) 140 °C, 5 min.

Table 1. Condensations of Alkylamines and Amino Acids with NDA

			[NMI] (%)			
entry	amino acid	NMI	closed	open	[NDI] (%)	yield (%)
1	propargylamine	**2a**	100	0	0	78
2	2-ethyl-*n*-butylamine	**2b**	100	0	0	86
3[a]	(*S*)-2-aminoheptane	**2c**	100	0	0	59
4[a]	(*R*)-2-aminoheptane	**2d**	100	0	0	44
5	4-aminomethylpyridine	**2e**	100	0	0	89
6	(*S*)-3-amino-1,2-propanediol	**2f**	100	0	0	69
7	*N*-alloc-ethylenediamine	**2g**	100	0	0	88
8	H-L-Asn(Trt)-OH	**2h**	61	39	0	87[b]
9	H-L-Cys(Trt)-OH	**2i**	81	19	0	91[b]
10	H-L-Cys(Trt)-NH_2	**2j**	56	44	0	87[b]
11	H-L-Gln(Trt)-OH	**2k**	57	43	0	85[b]
12	H-L-His(Trt)-OMe	**2l**	49	51	0	81[b]
13	H-L-Tyr(OBn)-OMe	**2m**	68	32	0	90[b]
14	H-L-Asp(OBn)-OBn	**2n**	70	22	8	85[c]
15	H-L-Cys(tBu)-OH	**2o**	76	8	16	73[c]
16	H-L-Glu-OtBu	**2p**	57	4	39	80[c]
17	H-L-Ile-OMe	**2q**	54	3	43	83[c]
18	H-L-Ile-OtBu	**2r**	53	9	38	79[c]
19	H-L-Phe-OtBu	**2s**	78	15	7	86[c]
20	H-L-Tyr-OtBu	**2t**	76	13	11	78[c]
21	H-L-Tyr-OH	**2u**	28	11	61	73[c]
22	H-L-Tyr(OMe)-OH	**2v**	66	14	20	84[c]

[a] Heated for 15 min at 140 °C. [b] Yield calculated on the basis of NDA as the sum of the closed and open NMIs. [c] Conversion calculated on the basis of the NMI and NDI mixture.

after heating at 75 °C showed the monoreacted open-ring amide/carboxylic acid intermediate to be the major product (Figure 1a, **I**).

However, even upon further heating under high microwave power (140 °C for 2 h with continuous nitrogen cooling and a microwave power input of 150−200W), the ^{1}H NMR spectrum of the mixture indicated the presence of the same intermediate (**I**) along with monodecarboxylated products. No significant quantities of NDIs or other disubstituted derivatives were observed under the reaction conditions.

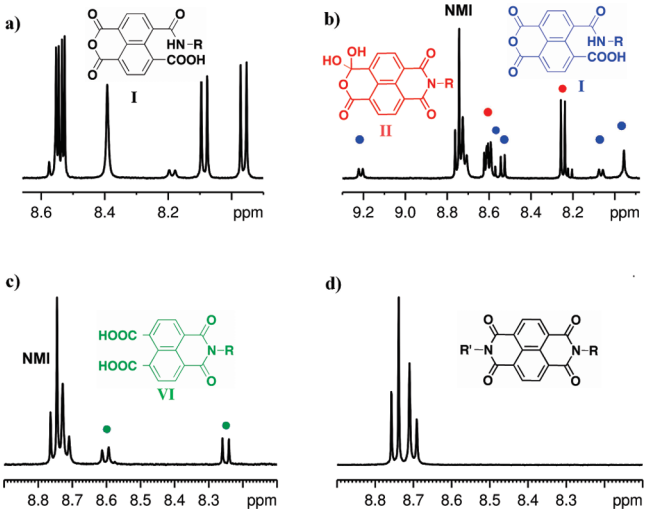


Figure 1. ^{1}H NMR spectra of the aromatic naphthalene region: (a) R = adamantanyl; (b) R = $CH(COOH)CH_2STrt$, after 5 min at 40 °C; (c) R = $CH(COOH)CH_2STrt$, after 5 min at 40 °C and 5 min at 140 °C (**2i**); (d) R = $CH(COOH)CH_2STrt$, R′ = $CH(CONH_2)CH(CH_3)CH_2CH_3$ (**3n**).

For all the aliphatic and aromatic amines tested, with the exception of adamantamine, carrying out the reaction at 140 °C only leads to the formation of a statistical mixture of dianhydride, monoimide, and diimide in a 1:2:1 ratio, which highlights the importance of this stepwise process.

Due to our work with amino acid-derived NDI-based nanotubes and catenanes,[6] we investigated the synthesis of NMIs using amino acids and amino acid esters as starting materials (**2h−v**), according to Scheme 1. Surprisingly, the amino acids, whose α-carbons are tertiary, gave yields and purities comparable to those of amines with secondary α-carbons. In contrast to the NMI synthesis starting from aliphatic amines, this procedure requires the reaction to be carried out first at 40 °C rather than 75 °C; temperatures above 40 °C led to the formation of the undesired disubstituted NDIs. This suggests that the COOR group of the amino acid derivatives assists in the collapse of the tetrahedral intermediate formed in the first steps of the imide formation.

The amino acid-derived NMIs were obtained as a mixture of open and closed forms, and their ratios were determined by ^{1}H NMR integration. The ^{1}H NMR spectrum of the naphthalene aromatic region is shown in Figure 1c: due to their symmetry, only two proton signals are observed for both the closed and the open forms. The closely spaced doublets (8.75 ppm) represent the closed form of the monoimide, and the further spaced doublets (8.6 and 8.25 ppm) represent the open form (Figure 1c, **VI**). Performing the reaction at only 40 °C but for a longer period of time (30 min instead of 5 min) proved to be particularly effective at reducing the proportion of open monoimide (**VI**). Increasing the temperature to 140 °C in the second stage of the reaction (Scheme 1) produces the NMI in only 5 min, while an increase in the proportion of the open NMI byproduct (**VI**) is observed. The percentage of this open form of the monoimide is higher for the reaction with amino acid derivatives than for the reaction with amines. We speculate that the addition of triethylamine in the former reaction promotes, at high temperatures, the formation of hydroxide ions which attack any unreacted anhydride moieties, leading to the formation of open byproduct.

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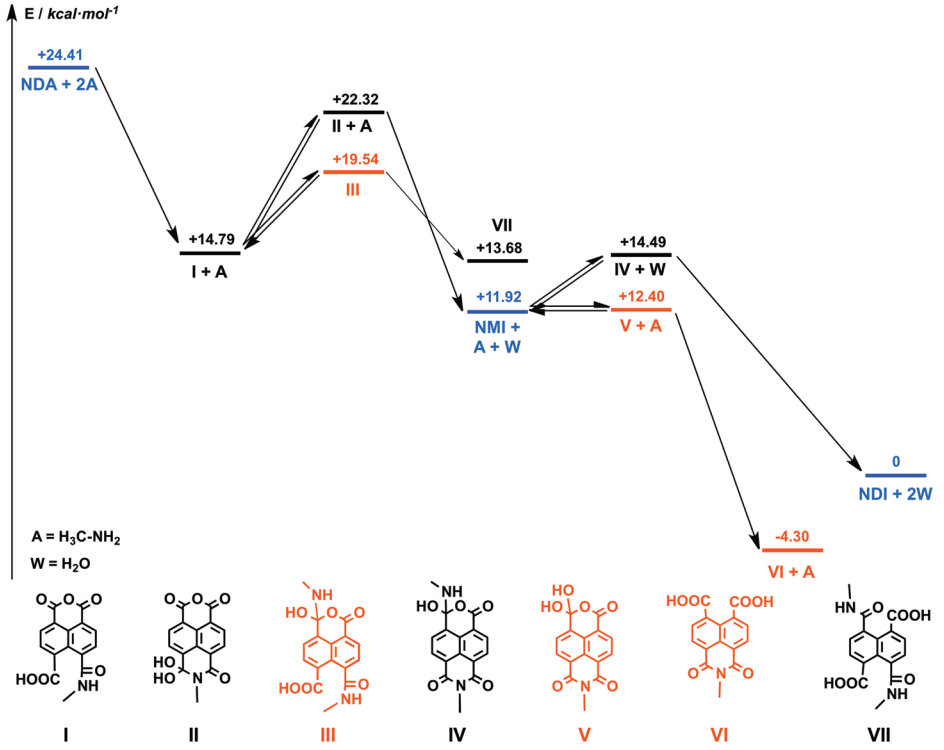
Scheme 2. Normalized Energy Diagram for the Intermediates in the Reaction Pathway[a]



[a] Hyperchem 8.0, ab initio level: geometry optimization using direct SCF calculation, the 6-31G* basis set, and 0.05 kcal/mol convergence criteria. The red energy levels correspond to experimentally observed intermediates, while the blue ones are for the starting materials and the two products, NMI and NDI.

This one-pot procedure for the synthesis of amino acid-derived NMIs proved to be reliable and efficient, allowing the isolation of monoimide without extensive purification efforts. The synthesis was successfully scaled up (5 g of **1**) without compromising the yield or purity.

The NMI syntheses which produced undesired NDI byproducts (Table 1, entries 14−22) led us to further explore the determinants of the observed monoimide/diimide selectivity. On comparing entries 8−22 in Table 1, we conclude that a higher degree of selectivity in favor of the monoimide was obtained when the amino acid derivatives contained aromatic side chains. For amino acids containing the trityl group (Table 1, entries 8−12), 100% selectivity for the monoimide was observed. The product mixture contained 70−90% NMI when amino acids with benzyl- and *tert*-butyl-protected side chains were used. The lowest selectivity was obtained for the amino acids containing all alkyl side chains. Also the amino acid esters gave higher yields of the monoimide than the corresponding amino acids. This trend can be rationalized by the solubility of the amino acid derivative and its reactivity toward NDA in DMF at room temperature. The NDA is insoluble in DMF at room temperature, but is rapidly solubilized by an amino acid derivative containing aromatic side chains, which is itself soluble in DMF. We speculate that the dissolution of NDA in DMF is probably due to $\pi-\pi$ interactions between its extended aromatic core and the amino acid aromatic side chains. This in turn leads to the formation of an open amide/carboxylic acid intermediate observed through LC−MS and ^{1}H NMR (Figure 1a).

In the cases where sonication and heating were required to completely dissolve the reagents, a strong preference for the formation of the NDI was observed. We propose that intermediate **I** (Figure 1 and Scheme 2) and indeed the NMI are less reactive toward ring-opening of the second anhydride by another molecule of the amino acid than the unreacted NDA. The importance of solubility is best illustrated by the three tyrosine derivatives investigated: H-L-Tyr-OtBu, H-L-Tyr(OMe)-OH, and H-L-Tyr-OH, which have similar π-surfaces (Table 1, entries 20−22). Their solubility profiles in DMF at room temperature are very different: the first and second, being an ester and ether, respectively, show excellent solubility in DMF, whereas the third is only partially soluble. As expected, the first and second derivatives rapidly solubilized NDA in DMF and gave better selectivity toward the NMI (89% and 80%, respectively) compared to tyrosine (39%), as shown in Table 1 (entries 20−22). The enhanced solubility of NDA in DMF due to its interaction with a suitable amino acid leads to a 1:1 mixture of NDA and the amino acid in solution and hence promotes the selective formation of the NMI.

Molecular modeling was performed at the ab initio level for the possible intermediates of the reaction between NDA (**1**) and methylamine. The latter compound was used because of its limited number of conformations, and it allows us to study the selectivity observed irrespective of the steric hindrance at the α-carbon or the solubility (Scheme 2). The modeling is in agreement with the experimental findings: the NMI is of intermediate energy between the NDA and NDI, and therefore, direct high-temperature heating leads to a mixture of the three compounds. The selectivity for the NMI lies in the steps involving intermediates **I**, **II**, and **III**: compound **II**, although slightly higher in energy than **III**, is formed via an intramolecular process and is therefore favored kinetically. The following steps involve quasi-

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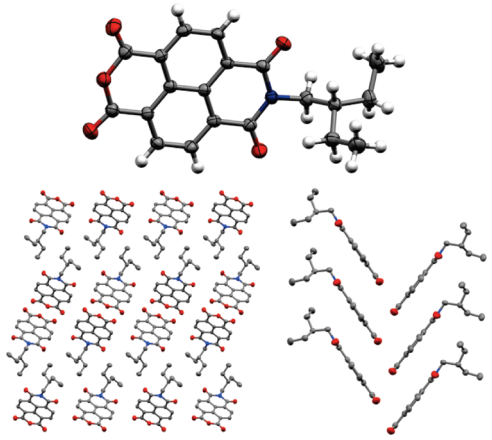

Figure 2. Side and crystal-packing views of **2b**. The thermal ellipsoids are scaled at the 50% probability level. All hydrogen atoms in the crystal-packing views have been removed for clarity.

irreversible reactions leading to NMI and **VII**, respectively, with the former compound being thermodynamically favored. Under both stringent reaction conditions (140 °C) and in the presence of triethylamine base, the NMI can react further with the hydroxide ions to produce **V**, which, in turn, leads to the formation of **VI**. This hypothesis is consistent with the observation that, for NMI synthesis with amino acids where triethylamine base and heating at 140 °C are employed, byproducts of type **VI** are observed in significant proportions.

Structural proof of the NMI **2b** came from single-crystal X-ray diffraction analysis of crystals grown by slow evaporation of an acetone solution. The single molecule and packing geometry of **2b** are shown in Figure 2. The compound adopts a $P2_1/c$ space group where the unit cell contains molecules arranged in parallel fashion. The packing orientation of **2b** suggests C═O−π-type interactions,[9] with a nonconjugating lone pair of the anhydride oxygen oriented directly toward the π-system of the anhydride moiety of a neighboring molecule. The C═O···π distance is 3.06 Å, while the π-stacking distance is 3.54 Å.

The synthesis of desymmetrised NDIs **3a**−**v** is outlined in Scheme 1. A wider variety of compounds containing amine functionalities were investigated for the second condensation (Table 2). Triethylamine was required for the reactions with amino acids to enable the condensation of the amine by deprotonating the zwitterion. Aromatic amines gave poorer yields compared to alkylamines due to their decreased nucleophilicity. They also required longer reaction times (15 min at 140 °C), which is consistent with the hypothesis that the electronic properties of the attacking amine also have a significant influence on the yield. The presence of the open form of the NMI (**I**) did not hinder the second condensation, as no peaks corresponding to the unreacted open NMI were observed in the ^{1}H NMR spectra of the final N-desymmetrized NDIs (Figure 1d).

In conclusion, a diverse family of naphthalenemonoimides and N-desymmetrized naphthalenediimides were synthesized and isolated via straightforward synthesis and purification. The reactions were critically influenced by the chemical nature of the amine nucleophile, in particular its steric and electronic properties at the α-carbon, as well as by its solubility and the ability to form noncovalent interactions with NDA in the reaction conditions. The selectivity observed in favor of the monoimides over a statistical mixture was rationalized by theoretical calculations of the energies of the intermediates in the reaction pathway.

Table 2. Condensations of Alkylamines and Amino Acids with NMIs

entry	NMI	amine	NDI	time[a] (min)	yield (%)
1	**2a**	(*S*)-2-aminoheptane	**3a**	15	41
2	**2a**	(*R*)-2-aminoheptane	**3b**	15	44
3	**2b**	(*S*)-2-aminoheptane	**3c**	15	32
4	**2b**	(*R*)-2-aminoheptane	**3d**	15	28
5	**2a**	2-ethyl-*n*-butylamine	**3e**	5	69
6	**2b**	H-L-Cys(Trt)-OH	**3f**	5	61
7	**2a**	H-L-Cys(Trt)-OH	**3g**	5	73
8	**2b**	H-L-Ile-OH	**3h**	5	62
9	**2b**	H-L-Trp-OH	**3i**	5	82
10	**2b**	4-iodoaniline	**3j**	15	38
11	**2b**	4-ethynylaniline	**3k**	15	33
12	**2i**	2-ethylbutylamine	**3l**	5	94
13	**2i**	H-L-Phe(4-Br)-OH	**3m**	5	90
14	**2i**	H-L-Ile-NH_2	**3n**	5	87
15	**2i**	H-L-Cys(Trt)-OMe	**3o**	5	89
16	**2i**	H-L-Cys(Trt)-NH_2	**3p**	5	85
17	**2i**	H-L-Lys(Boc)-OH	**3q**	5	87
18	**2j**	H-L-Gly-OMe	**3r**	5	94
19	**2h**	H-L-Gly-OMe	**3s**	5	90
20	**2n**	2-ethylbutylamine	**3t**	5	91
21	**2n**	H-L-Gly-OMe	**3u**	5	93
22	**2n**	H-L-Phe-OtBu	**3v**	5	84

[a] For entries 1−12, the reactions were carried out in two stages, first heating at 75 °C for 5 min followed by heating for the reported duration at 140 °C.

EXPERIMENTAL SECTION

General Information. All solvents used were of reagent quality and purchased commercially. All purchased starting materials were used without further purification. The microwave reactor used for this study (CEM Discover) was purchased from CEM Corp. NMR spectra were recorded on 400 MHz instruments and referenced to the solvent. All spectra were recorded at 298 K. ^{1}H NMR spectral data are reported as follows: chemical shift in parts per million on the δ scale, integration, multiplicity, coupling constants (Hz), and assignments. ^{13}C NMR spectral data are reported as follows: chemical shifts in parts per million on the δ scale and carbon environments determined from DEPT spectra. All spectra were referenced to their respective solvent residual peaks.[10]

General Procedure A. Synthesis of Naphthalenemonoimide Derivatives of Alkylamines (2a−g). 1,4,5,8-Naphthalenetetracarboxylic dianhydride and the corresponding amine (1 equiv) were suspended in dry dimethylformamide (5 mL) in a pressure-tight microwave tube. The suspension was sonicated until the mixture became homogeneous. The reaction mixture was heated under microwave irradiation for 5 min at 75 ± 5 °C and then for 5−15 min at 140 ± 5 °C. The solvent was removed under reduced pressure, and each reaction was worked up using a suitable method.

General Procedure B. Synthesis of Naphthalenemonoimide Derivatives of α-Amino Acids (2h−v). 1,4,5,8-Naphthalenetetracarboxylic dianhydride and the corresponding α-amino acid (1 equiv) were suspended in dry DMF (5 mL) in a pressure-tight microwave tube. To this suspension was added dry Et_3N (1 equiv).

The suspension was sonicated until the mixture became homogeneous. The reaction mixture was heated under microwave irradiation for 5 min at 40 ± 5 °C and then for 5 min at 140 ± 5 °C. The solvent was removed under reduced pressure to give a brown residue which was then suspended in acetone. The suspension was added slowly to vigorously stirred 1 M HCl(aq). The precipitate thus obtained was filtered and washed with water and dried in vacuo to yield the product as a colored solid.

General Procedure C. Synthesis of Asymmetrical Naphthalenediimide Derivatives of Mixed Alkylamines and α-Amino Acids (3a−k). The naphthalenemonoimide derivative, synthesized according to general procedure A, and the corresponding second amine (1 equiv) were suspended in dry DMF (5 mL). To this suspension was added dry Et_3N (1 equiv). The suspension was sonicated until the mixture became homogeneous. The reaction mixture was heated under microwave irradiation for 5 min at 75 ± 5 °C and then 5−15 min at 140 ± 5 °C. The solvent was removed under reduced pressure, and each reaction mixture was worked up using a suitable method.

General Procedure D. Synthesis of Asymmetrical Naphthalenediimide Derivatives of Mixed Alkylamines and α-Amino Acids (3l−v). The naphthalenemonoimide derivative, synthesized according to general procedure A, and the corresponding second amine or α-amino acid (1 equiv) were suspended in dry DMF (5 mL). To this suspension was added dry Et_3N (1 equiv). The suspension was sonicated until the mixture became homogeneous. The reaction mixture was heated under microwave irradiation for 5 min at 140 ± 5 °C. The solvent was removed under reduced pressure to give a brown residue which was then suspended in acetone. The suspension was added slowly to vigorously stirred 1 M HCl(aq). The precipitate thus obtained was filtered and washed with water and dried in vacuo to yield the product as a colored solid.

Workup and Characterization Data: Naphthalenemonoimides. 2a: The reaction was performed on 0.932 mmol (250 mg) of 1,4,5,8-naphthalenetetracarboxylic dianhydride (NDA) and 0.932 mmol (60 μL) of propargylamine using general procedure A. Workup: the brown residue was suspended in acetone and the suspension added slowly to vigorously stirred 1 M HCl(aq). The precipitate was filtered and washed with water and dried in vacuo to yield the product as a light brown solid (223 mg, 78%). ^{1}H NMR (400 MHz, d_6-DMSO): 3.21 (1H, t, J = 2.4 Hz), 4.82 (2H, d, J = 2.4 Hz), 8.69−8.74 (4H, m). ^{13}C NMR (100 MHz, d_6-DMSO): 26.7 (CH_2), 73.4 (C), 73.5 (C), 124.6 (C), 126.3 (C), 126.7 (C), 130.7 (CH), 131.6 (CH), 131.8 (C), 159.4 (C), 161.7 (C). Anal. Calcd for $3C_{17}H_7NO_5 \cdot H_2O$: C, 65.60; H, 2.48; N, 4.50. Found: C, 65.67; H, 2.56; N, 4.36. Mp: 251 °C dec.

2b: The reaction was performed on 2.237 mmol (600 mg) of NDA and 2.237 mmol (291 μL) of 2-ethyl-*n*-butylamine using general procedure A. Workup: the brown residue was suspended in acetone and the suspension added slowly to vigorously stirred 1 M HCl(aq). The precipitate was filtered and washed with water and dried in vacuo to yield the product as a light brown solid (608 mg, 77%). The experiment was successfully scaled up to 5 g of NDA (product yield 5.610 g, 86%). ^{1}H NMR (400 MHz, d_6-DMSO): 0.89 (6H, t, J = 7.4 Hz), 1.34 (4H, m), 1.81 (1H, m), 4.02 (2H, d, J = 7.2 Hz), 8.71 (4H, m). ^{13}C NMR (100 MHz, d_6-DMSO): 10.5 (CH_3), 23.0 (CH_2), 30.7 (CH), 43.5 (CH_2), 123.7 (C), 126.1 (C), 127.0 (C), 130.5 (C), 131.6 (CH), 131.8 (CH), 159.7 (C), 162.7 (C). Anal. Calcd for $2C_{20}H_{17}NO_5 \cdot H_2O$: C, 66.66; H, 5.03; N, 3.89. Found: C, 66.81; H, 4.71; N, 3.65. Mp: 212 °C dec.

2c: The reaction was performed on 0.746 mmol (200 mg) of NDA and 0.746 mmol (112 μL) of (*S*)-2-aminoheptane using general procedure A. Workup: the brown residue was suspended in acetone and the suspension added slowly to vigorously stirred 1 M HCl(aq). The precipitate was filtered and washed with water and dried in vacuo to yield the product as a light brown solid (162 mg, 59%). ^{1}H NMR (400 MHz, d_6-DMSO): 0.80 (3H, m), 1.23 (8H, m), 1.52 (3H, d, J = 6.9 Hz), 5.13 (1H, m), 8.68 (2H, d, J = 7.6 Hz), 8.71 (2H, d, J = 7.6 Hz). Anal. Calcd for $4C_{21}H_{19}NO_5 \cdot$DMF: C, 68.09; H, 5.45; N, 4.56. Found: C, 68.03; H, 5.84; N, 4.17. Mp: 149 °C dec.

2d: The reaction was performed on 0.746 mmol (200 mg) of NDA and 0.746 mmol (112 μL) of (*R*)-2-aminoheptane using general procedure A. Workup: the brown residue was suspended in acetone and the suspension added slowly to vigorously stirred 1 M HCl(aq). The precipitate was filtered and washed with water and dried in vacuo to yield the product as a light brown solid (88 mg, 32%). ^{1}H NMR (400 MHz, d_6-DMSO): 0.80 (3H, m), 1.24 (8H, m), 1.52 (3H, d, J = 6.9 Hz), 5.13 (1H, m), 8.68 (2H, d, J = 7.6 Hz), 8.71 (2H, d. J = 7.6 Hz). Anal. Calcd for $4C_{21}H_{19}NO_5 \cdot$DMF$\cdot(CH_3)_2CO$: C, 67.87; H, 5.63; N, 4.40. Found: C, 68.16; H, 5.86; N, 4.33. Mp: 148 °C dec.

2e: The reaction was performed on 0.746 mmol (200 mg) of NDA and 0.746 mmol (75 μL) of 4-(aminomethyl)pyridine using general procedure A. Workup: the brown residue was suspended in water, filtered, and washed with copious water. The solid was dried in vacuo to yield the product as a brown solid (201 mg, 75%). ^{1}H NMR (400 MHz, d_6-DMSO): 5.29 (2H, s), 7.41 (2H, d, J = 5.9 Hz), 8.49 (2H, m), 8.72 (4H, m). ^{13}C NMR (100 MHz, d_6-DMSO): 42.8 (CH_2), 122.2 (CH), 124.0 (C), 126.4 (C), 127.1 (C), 128.5 (C), 130.7 (CH), 131.8 (CH), 145.7 (C), 149.6 (CH), 159.6 (C), 162.6 (C). Anal. Calcd for $5C_{20}H_{10}N_2O_5 \cdot 2DMF\cdot 2H_2O$: C, 64.50; H, 3.47; N, 8.52. Found: C, 64.35; H, 3.37; N, 8.20. Mp: 279 °C dec.

2f: The reaction was performed on 0.746 mmol (200 mg) of NDA and 0.746 mmol (68 mg) of (*S*)-3-amino-1,2-propanediol using general procedure A. Workup: the reaction mixture in DMF was added directly to diethyl ether. The precipitate was filtered and washed with diethyl ether to yield the product as a light brown solid (129 mg, 51%). ^{1}H NMR (400 MHz, d_6-DMSO): 3.44 (2H, m), 3.94 (1H, m), 4.03 (1H, dd, J_1 = 12.9 Hz, J_2 = 4.6 Hz), 4.26 (1H, dd, J_1 = 12.9 Hz, J_2 = 8.6 Hz), 4.61 (1H, m), 4.85 (1H, d, J = 5.0 Hz), 8.68 (2H, d, J = 7.6 Hz), 8.71 (2H, d, J = 7.6 Hz). ^{13}C NMR (100 MHz, d_6-DMSO): 43.9 (CH_2), 64.5 (CH), 68.2 (CH_2), 123.7 (CH), 126.2 (C), 127.3 (C), 128.5 (C), 130.3 (CH), 131.8 (CH), 159.8 (C), 162.7 (C). Anal. Calcd for $2C_{17}H_{11}NO_7 \cdot H_2O$: C, 58.29; H, 3.45; N, 4.10. Found: C, 57.94; H, 3.58; N, 4.21. Mp: 145 °C dec.

2g:The reaction was performed on 0.746 mmol (200 mg) of NDA and 0.746 mmol (135 mg) of *N*-alloc-ethylenediamine hydrochloride using general procedure A. Workup: the brown residue was suspended in acetone and the suspension added slowly to vigorously stirred 1 M HCl(aq). The precipitate was filtered and washed with water and dried in vacuo to yield the product as a light brown solid (258 mg, 88%). ^{1}H NMR (400 MHz, d_6-DMSO): 3.37 (2H, q, J = 5.8 Hz), 4.18 (2H, t, J = 5.8 Hz), 4.37 (2H, d, J = 5.2 Hz), 5.08 (1H, dd, J_1 = 1.6 Hz, J_2 = 10.4 Hz), 5.19 (1H, dd, J_1 = 1.6 Hz, J_2 = 17.2 Hz), 5.79 (1H, m), 7.30 (1H, t, J = 6.1 Hz), 8.68 (2H, d, J = 7.6 Hz), 8.71 (2H, d, J = 7.6 Hz). ^{13}C NMR (100 MHz, d_6-DMSO): 38.0 (CH_2), 40.2 (CH_2), 64.1 (CH_2), 116.6 (CH_2), 123.7 (C), 126.1 (C), 127.2 (C), 128.4 (C), 130.3 (CH), 131.8 (CH), 133.7 (CH), 156.2 (C), 159.7 (C), 162.6 (C). Anal. Calcd for $5C_{20}H_{14}N_2O_7 \cdot H_2O$: C, 60.36; H, 3.65; N, 7.04. Found: C, 60.38; H, 3.79; N, 7.29. Mp: 233 °C dec.

2h: The reaction was performed on 0.746 mmol (200 mg) of NDA and 0.746 mmol (279 mg) of H-L-Asn(Trt)-OH using general procedure A. Yield: 405 mg, 87%. ^{1}H NMR (400 MHz, d_6-DMSO): 2.81−2.87 (1H, dd, J = 6.51 Hz, J = 15.4 Hz), 3.52−3.57 (1H, dd, J = 7.54 Hz, J = 15.4 Hz), 6.03−6.08 (1H, dd, J = 6.86 Hz, J = 14.4 Hz), 7.10−7.13 (15H, m), 8.70−8.75 (4H, 2d, 7.5 Hz), 8.76−8.82 (1H, 2s). ^{13}C NMR (100 MHz, d_6-DMSO): 170.5, 168.9, 168.4, 162.3, 161.9, 159.7, 144.7, 137.1, 131.8, 131.0, 129.4, 128.4, 127.3, 126.3, 124.3, 123.9, 69.2, 50.2, 49.9, 35.9. HRMS (ESI+) (m/z): calcd for $C_{37}H_{25}N_2O_8$ $[M + H]^+$, 625.1611; found, 625.1603. HRMS (ESI+) (m/z): calcd for $C_{37}H_{27}N_2O_9$ $[M + H]^+$, 643.1717; found, 643.1714.

2i: The reaction was performed on 0.746 mmol (200 mg) of NDA and 0.746 mmol (271 mg) of H-L-Cys(Trt)-OH using general procedure

A. Yield: 416 mg, 91%. The experiment was successfully scaled up to 5 g of NDA (6.09 g, 90%). ^{1}H NMR (400 MHz, *d*-$CDCl_3$): 3.20−3.29 (2H, m), 5.51−5.55 (1H, m), 7.13−7.34 (15H, m), 8.76 (4H, 2d, J = 8 Hz). ^{13}C NMR (100 MHz, d_6-DMSO): 169.5, 168.7, 162.7, 162.2, 160.1, 144.5, 132.3, 131.9, 130.0, 129.4, 129.1, 129.0, 128.4, 127.3, 126.4, 126.1, 125.1, 66.9, 66.8 52.8, 36.2, 31.2, 30.6. HRMS (ESI+) (m/z): calcd for $C_{36}H_{23}NO_7SNa$ $[M + Na]^+$, 636.1087; found, 636.1078. HRMS (ESI+) (m/z): calcd for $C_{36}H_{25}NO_8SNa$ $[M + Na]^+$, 654.1199; found, 654.1207.

2k: The reaction was performed on 0.746 mmol (200 mg) of NDA and 0.746 mmol (290 mg) of H-L-Gln(Trt)-OH using general procedure A. Yield: 405 mg, 85%. ^{1}H NMR (400 MHz, d_6-DMSO): 2.24−2.31 (2H, m), 2.41−2.46 (2H, m), 5.56−5.60 (1H, m), 7.12−7.27(15H, m), 8.43−8.47 (1H, 2s), 8.76 (4H, s). ^{13}C NMR (100 MHz, d_6-DMSO): 171.2, 170.6, 170.5, 168.4, 162.7, 162.3, 159.7, 144.8, 137.1, 131.9, 131.2, 130.8, 129.4, 128.5, 127.4, 126.4, 126.3, 124.3, 124.0, 69.2, 53.3, 52.9, 32.6, 32.4, 24.3, 24.0. HRMS (ESI+) (m/z): calcd for $C_{38}H_{27}N_2O_8$ $[M + H]^+$, 639.1767; found, 639.1755. HRMS (ESI+) (m/z): calcd for $C_{38}H_{29}N_2O_9$ $[M + H]^+$, 657.1873; found, 657.1878.

2l: The reaction was performed on 0.746 mmol (200 mg) of NDA and 0.746 mmol (334 mg) of H-L-His(Trt)-OMe·HCl using general procedure A. Yield: 399 mg, 81%. ^{1}H NMR (400 MHz, d_6-DMSO): 3.41−3.47 (2H, m), 3.69−3.70 (3H, 2s), 5.97−6.00 (1H, m), 6.97−7.07 (7H, m), 7.25−7.39 (10H, m), 8.82 (4H, 2d, J = 6.4 Hz). ^{13}C NMR (100 MHz, d_6-DMSO): 168.5, 168.3, 162.4, 162.2, 140.3, 140.1, 137.6, 136.5, 131.3, 129.4, 129.1, 128.5, 125.9, 125.6, 123.4, 121.5, 77.3, 52.7, 52.5, 34.1, 30.8. HRMS (ESI+) (m/z): calcd for $C_{40}H_{28}N_3O_7$ $[M + H]^+$, 662.1927; found, 662.1923. HRMS (ESI+) (m/z): calcd for $C_{40}H_{30}N_3O_8$ $[M + H]^+$, 680.2027; found, 680.2035.

2m: The reaction was performed on 0.746 mmol (200 mg) of NDA and 0.746 mmol (240 mg) of H-L-Tyr(OBn)-OMe·HCl using general procedure A. Yield: 359 mg, 90%. ^{1}H NMR (400 MHz, d_6-DMSO): 3.39−3.46 (1H, m), 3.60−3.68 (1H, m), 3.72−3.73 (3H, 2s), 4.94−4.95 (2H, 2s), 5.97−6.06 (1H, m), 6.76−6.78 (1H, d, J = 9.6 Hz), 7.13−7.17 (2H, m), 7.27−7.38 (5H, m), 8.76−8.83 (4H, 2d, J = 8 Hz). ^{13}C NMR (100 MHz, d_6-acetone): 170.2, 168.8, 163.4, 162.9, 160.3, 158.5, 138.3, 133.2, 132.1, 131.5, 131.1, 130.5, 130.4, 129.2, 128.5, 128.4, 128.3, 127.6, 125.3, 115.5, 70.2, 55.7, 55.4, 52.8, 52.6, 34.5. HRMS (ESI+) (m/z): calcd for $C_{31}H_{22}NO_8$ $[M + H]^+$, 536.1345; found, 536.1342. HRMS (ESI+) (m/z): calcd for $C_{31}H_{24}NO_9$ $[M + H]^+$, 554.1451; found, 554.1446.

2n: The reaction was performed on 0.746 mmol (200 mg) of NDA and 0.746 mmol (261 mg) of H-L-Asp(OBn)-OBn·HCl using general procedure A. Yield: 358 mg, 85%. Monoimide:diimide = 92:8. ^{1}H NMR (400 MHz, d_6-DMSO): 3.07−3.13 (1H, dd, J = 4.8 Hz, J = 16 Hz), 3.40−3.47 (1H, dd, J = 8.8 Hz, J = 16 Hz), 5.08−5.17 (4H, m), 6.15−6.22 (1H, m), 7.21−7.30 (10H, m), 8.70−873 (4H, m). ^{13}C NMR (100 MHz, d_6-DMSO): 170.1, 168.5, 162.1, 159.7, 135.8, 135.5, 131.8, 131.2, 128.7, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 126.1, 124.7, 66.9, 66.1, 66.0, 49.7, 33.8. HRMS (ESI+) (m/z): calcd for $C_{32}H_{22}NO_9$ $[M + H]^+$, 564.1295; found, 564.1301. HRMS (ESI+) (m/z): calcd for $C_{32}H_{24}NO_{10}$ $[M + H]^+$, 582.1400; found, 582.1413.

2o: The reaction was performed on 0.746 mmol (200 mg) of NDA and 0.746 mmol (132 mg) of H-L-Cys(tBu)-OH using general procedure A. Yield: 247 mg, 73%. Monoimide:diimide = 84:16. ^{1}H NMR (400 MHz, *d*-$CDCl_3$): 1.3 (9H, s), δ3.47−3.52 (2H, m), 5.94−5.98 (1H, m), 8.86 (4H, s). ^{13}C NMR (100 MHz, d_6-DMSO): 169.9, 169.8, 162.4, 162.2, 162.0, 159.7, 131.9, 131.4, 129.6, 128.7, 128.5, 126.0, 124.7, 123.7, 54.1, 53.7, 53.6, 42.4, 42.3, 30.6, 26.6. HRMS (ESI+) (m/z): calcd for $C_{21}H_{18}NO_7S$ $[M + H]^+$, 428.0804; found, 428.0801. HRMS (ESI+) (m/z): calcd for $C_{21}H_{20}NO_8S$ $[M + H]^+$, 446.0910; found, 446.0924. HRMS (ESI+) (m/z): calcd for $C_{28}H_{31}N_2O_8S_2$ $[M + H]^+$, 587.1516; found, 587.1517.

2p: The reaction was performed on 0.746 mmol (200 mg) of NDA and 0.746 mmol (179 mg) of H-L-Glu-OtBu·HCl using general procedure A. Yield: 314 mg, 80%. Monoimide:diimide = 61:39. ^{1}H NMR (400 MHz, *d*-$CDCl_3$): 1.43−1.44 (9H, 2s), 2.38−2.53 (2H, m), 2.63−2.71 (2H, m), 5.60−5.64 (1H, m), 8.82 (4H, s). ^{13}C NMR data (100 MHz, d_6-DMSO): 174.1, 167.9, 162.5, 162.4, 159.7, 131.8, 131.0, 128.6, 126.5, 126.3, 126.2, 124.3, 81.3, 53.8, 53.6, 30.8, 30.3, 27.5, 23.5. HRMS (ESI+) (m/z): calcd for $C_{23}H_{20}NO_9$ $[M + H]^+$, 454.1133; found, 454.1127. HRMS (ESI+) (m/z): calcd for $C_{23}H_{21}NO_{10}Na$ $[M + Na]^+$, 494.1063; found, 494.1062. HRMS (ESI+) (m/z): calcd for $C_{32}H_{35}N_2O_{12}$ $[M + H]^+$, 639.2190; found, 639.2194.

2q: The reaction was performed on 0.746 mmol (200 mg) of NDA and 0.746 mmol (135 mg) of H-L-Ile-OMe·HCl using general procedure A. Yield: 279 mg, 83%. Monoimide:diimide = 57:43. ^{1}H NMR (400 MHz, *d*-$CDCl_3$): 0.85−0.87 (3H, m), 0.99−1.06 (1H, m), 1.29−1.30 (4H, m), 2.60−2.66 (1H, m), 3.71−3.72 (3H, 2s), 5.41−5.43 (1H, m), 8.85 (4H, s). ^{13}C NMR (100 MHz, d_6-DMSO): 169.2, 169.1, 162.5, 162.4, 159.6, 131.9, 131.6, 128.6, 126.5, 126.1, 125.7 124.6, 57.7, 57.6, 52.2, 33.3, 33.2, 30.7, 24.6, 17.7, 10.9. HRMS (ESI+) (m/z): calcd for $C_{21}H_{18}NO_7$ $[M + H]^+$, 396.1083; found, 396.1095. HRMS (ESI+) (m/z): calcd for $C_{21}H_{20}NO_8$ $[M + H]^+$, 414.1189; found, 414.1201. HRMS (ESI+) (m/z): calcd for $C_{28}H_{31}N_2O_8$ $[M + H]^+$, 523.2080; found, 523.2073.

2r: The reaction was performed on 0.746 mmol (200 mg) of NDA and 0.746 mmol (167 mg) of H-L-Ile-OtBu·HCl using general procedure A. Yield: 296 mg, 79%. Monoimide:diimide = 62:38. ^{1}H NMR (400 MHz, d_6-DMSO): 0.91−0.94 (3H, m), 0.95−0.99 (1H, m), 1.17−1.19 (3H, m), 1.29−1.31 (9H, 2s), 2.43−2.46 (1H, m), 5.19−5.22 (1H, m), 8.73−8.77 (4H, 2d, J = 8 Hz). ^{13}C NMR (100 MHz, d_6-DMSO): 167.6, 162.5, 162.3, 159.6, 131.9, 131.4, 126.5, 126.0, 125.8, 125.7, 124.6, 81.1, 58.7, 58.6, 33.3, 27.5, 24.8, 17.9, 10.9. HRMS (ESI+) (m/z): calcd for $C_{24}H_{24}NO_7$ $[M + H]^+$, 438.1547; found, 438.1558. HRMS (ESI+) (m/z): calcd for $C_{24}H_{26}NO_8$ $[M + H]^+$, 456.1658; found, 456.1672. HRMS (ESI+) (m/z): calcd for $C_{34}H_{43}N_2O_8$ $[M + H]^+$, 607.3019; found, 607.3031.

2s: The reaction was performed on 0.746 mmol (200 mg) of NDA and 0.746 mmol (192 mg) of H-L-Phe-OtBu·HCl using general procedure A. Yield: 314 mg, 86%. Monoimide:diimide = 93:7. ^{1}H NMR (400 MHz, d_6-DMSO): 1.365 (9H, m), 3.29−3.34 (1H, m), 3.56−3.60 (1H, m), 5.86−5.90 (1H, m), 7.05−7.19 (5H, m), 8.70 (4H, s). ^{13}C NMR (100 MHz, d_6-DMSO): 167.9, 167.7, 161.9, 159.6, 137.7, 131.9, 131.4, 129.1, 128.7, 128.3, 126.5, 125.8, 125.6, 124.7, 81.63, 51.3, 34.3, 27.6. HRMS (ESI+) (m/z): calcd for $C_{27}H_{22}NO_7$ $[M + H]^+$, 472.1396; found, 472.1410. HRMS (ESI+) (m/z): calcd for $C_{27}H_{24}NO_8$ $[M + H]^+$, 490.1502; found, 490.1514. HRMS (ESI+) (m/z): calcd for $C_{40}H_{39}N_2O_8$ $[M + H]^+$, 675.2706; found, 675.2697.

2t: The reaction was performed on 0.746 mmol (200 mg) of NDA and 0.746 mmol (204 mg) of H-L-Tyr-OtBu·HCl using general procedure A. Yield: 297 mg, 78%. Monoimide:diimide = 89:11. ^{1}H NMR (400 MHz, d_6-acetone): 1.43−1.44 (9H, 2s), 3.35−3.41 (1H, m), 3.55−3.60 (1H, m), 5.89−5.93 (1H, m), 6.57 (2H, d, J = 9.2 Hz), 7.03 (2H, d, J = 8.4 Hz), 8.81 (4H, 2d, J = 6.4 Hz). ^{13}C NMR (100 MHz, d_6-acetone): 168.7, 162.9, 160.2, 156.7, 133.2, 132.0, 131.0, 130.5, 129.9, 129.1, 127.7, 127.5, 125.1, 115.9, 82.2, 56.7, 34.5, 28.2. HRMS (ESI+) (m/z): calcd for $C_{27}H_{22}NO_8$ $[M + H]^+$, 488.1345; found, 488.1345. HRMS (ESI+) (m/z): calcd for $C_{27}H_{24}NO_9$ $[M + H]^+$, 506.1451; found, 506.1460. HRMS (ESI+) (m/z): calcd for $C_{40}H_{39}N_2O_{10}$ $[M + H]^+$, 707.2605; found, 707.2609.

2u: The reaction was performed on 0.746 mmol (200 mg) of NDA and 0.746 mmol (135 mg) of H-L-Tyr-OH using general procedure A. Yield: 288 mg, 73%. Monoimide:diimide = 39:61. ^{1}H NMR (400 MHz, d_6-DMSO): 3.19−3.29 (1H, m), 3.44−3.49 (1H, m), 5.76−5.85 (1H, m), 6.44−6.50 (2H, m), 6.91−6.95 (2H, d), 8.69(4H, s). ^{13}C NMR (100 MHz, d_6-acetone): 170.3, 162.0, 161.8, 155.6, 131.8, 131.3, 129.8,

128.6, 127.7, 127.5, 126.0, 125.6, 124.6, 115.0, 54.8, 54.7, 33.3, 33.2. HRMS (ESI+) (m/z): calcd for $C_{23}H_{14}NO_8$ $[M + H]^+$, 432.0719; found, 432.0723. HRMS (ESI+) (m/z): calcd for $C_{23}H_{16}NO_9$ $[M + H]^+$, 450.0825; found, 450.0825. HRMS (ESI+) (m/z): calcd for $C_{32}H_{23}N_2O_{10}$ $[M + H]^+$, 595.1353; found, 595.1355.

2v: The reaction was performed on 0.746 mmol (200 mg) of NDA and 0.746 mmol (146 mg) of H-L-Tyr(Me)-OH using general procedure A. Yield: 300 mg, 84%. Monoimide:diimide = 80:20. ^{1}H NMR (400 MHz, d_6-acetone): 3.26−3.29 (1H, m), 3.51−3.55 (1H, m), 3.58−3.59 (3H, 2s), 5.79−5.87 (1H, m), 6.65−6.68 (2H, m), 7.06−7.09 (2H, d), 8.66−8.71 (4H, m). ^{13}C NMR (100 MHz, d_6-acetone): 170.3, 161.8, 159.5, 157.7, 131.8, 131.3, 129.9, 125.8, 125.6, 124.5, 113.6, 54.9, 54.8, 33.3. HRMS (ESI+) (m/z): calcd for $C_{24}H_{16}NO_8$ $[M + H]^+$, 446.0876; found, 446.0888. HRMS (ESI+) (m/z): calcd for $C_{24}H_{18}NO_9$ $[M + H]^+$, 464.0982; found, 464.0984. HRMS (ESI+) (m/z): calcd for $C_{34}H_{26}N_2O_{10}$ $[M + H]^+$, 623.1660; found, 623.1674.

Workup and Characterization Data: Naphthalenediimides.

3a: The reaction was performed on 0.328 mmol (100 mg) of **2a** and 0.328 mmol (49 μL) of (*S*)-2-aminoheptane using general procedure B. Workup: the brown residue was suspended in acetone and the suspension added slowly to vigorously stirred 1 M HCl(aq). The precipitate was filtered and washed with water and dried in vacuo to yield the product as a brown solid (54 mg, 41%). ^{1}H NMR (400 MHz, d_6-DMSO): 0.80 (3H, m), 1.23 (8H, m), 1.51 (3H, d, J = 6.9 Hz), 3.20 (1H, t, J = 2.4 Hz), 4.82 (2H, d, J = 2.4 Hz), 5.14 (1H, m), 8.69 (2H, d, J = 7.6 Hz), 8.71 (2H, d, J = 7.6 Hz). ^{13}C NMR (100 MHz, d_6-DMSO): 13.9 (CH_3), 17.9 (CH_3), 21.9 (CH_2), 26.0 (CH_2), 29.5 (CH_2), 31.0 (CH_2), 32.8 (CH_2), 49.3 (CH), 73.5 (CH), 78.8 (C), 125.6 (C), 126.0 (C), 126.2 (C), 126.9 (C), 130.5 (CH), 130.8 (CH), 161.9 (C), 162.9 (C). Anal. Calcd for $2C_{24}H_{22}N_2O_4 \cdot H_2O$: C, 70.06; H, 5.63; N, 6.81. Found: C, 70.32; H, 5.65; N, 6.58. Mp: 162 °C.

3b: The reaction was performed on 0.328 mmol (100 mg) of **2a** and 0.328 mmol (49 μL) of (*R*)-2-aminoheptane using general procedure B. Workup: the brown residue was suspended in acetone and the suspension added slowly to vigorously stirred 1 M HCl(aq). The precipitate was filtered and washed with water and dried in vacuo to yield the product as a brown solid (58 mg, 44%). ^{1}H NMR (400 MHz, d_6-DMSO): 0.80 (3H, m), 1.24 (8H, m), 1.51 (3H, d, J = 6.9 Hz), 3.20 (1H, t, J = 2.2 Hz), 4.82 (2H, d, J = 2.2 Hz), 5.14 (1H, m), 8.69 (2H, d, J = 7.6 Hz), 8.71 (2H, d, J = 7.6 Hz). ^{13}C NMR (100 MHz, d_6-DMSO): 13.9 (CH_3), 17.9 (CH_3), 21.9 (CH_2), 26.0 (CH_2), 29.5 (CH_2), 31.0 (CH_2), 32.8 (CH_2), 49.3 (CH), 73.5 (CH), 78.9 (C), 125.7 (C), 126.1 (C), 126.3 (C), 127.0 (C), 130.5 (CH), 130.8 (CH), 161.9 (C), 162.9 (C). Anal. Calcd for $2C_{24}H_{22}N_2O_4 \cdot H_2O$: C, 70.06; H, 5.63; N, 6.81. Found: C, 70.37; H, 5.70; N, 6.53. Mp: 162 °C.

3c: The reaction was performed on 0.213 mmol (75 mg) of **2b** and 0.213 mmol (32 μL) of (*R*)-2-aminoheptane using general procedure B. Workup: the brown residue was suspended in acetone and the suspension added slowly to vigorously stirred 1 M HCl(aq). The precipitate was filtered and washed with water and dried in vacuo to yield the product as a brown solid (31 mg, 32%). ^{1}H NMR (400 MHz, d_6-DMSO): 0.80 (3H, m), 0.89 (6H, t, J = 7.4 Hz), 1.23 (8H, m), 1.33 (4H, m), 1.51 (3H, d, J = 6.9 Hz), 1.80 (1H, m), 4.01 (2H, d, J = 7.2 Hz), 5.14 (1H, m), 8.65−8.68 (4H, m). ^{13}C NMR (100 MHz, d_6-DMSO): 10.5 (CH_3), 13.9 (CH_3), 18.0 (CH_3), 21.9 (CH_2), 23.0 (CH_2), 26.0 (CH_2), 31.0 (CH_2), 32.7 (CH_2), 38.8 (CH), 43.3 (CH_2), 49.2(CH_2), 126.0 (C), 126.1 (C), 126.2 (C), 126.6 (C), 130.5 (CH), 130.6 (CH), 162.97 (C), 163.02 (C). Anal. Calcd for $2C_{27}H_{32}N_2O_4 \cdot H_2O$: C, 70.87; H, 7.27; N, 6.12. Found: C, 71.21; H, 7.04; N, 6.30. Mp: 144 °C.

3d: The reaction was performed on 0.213 mmol (75 mg) of **2b** and 0.213 mmol (32 μL) of (*S*)-2-aminoheptane using general procedure B. Workup: the brown residue was suspended in acetone and the suspension added slowly to vigorously stirred 1 M HCl(aq). The precipitate was filtered and washed with water and dried in vacuo to yield the product as a brown solid (26 mg, 28%). ^{1}H NMR (400 MHz, d_6-DMSO): 0.80 (3H, m), 0.89 (6H, t, J = 7.5 Hz), 1.23 (8H, m), 1.33 (4H, m), 1.51 (3H, d, J = 6.9 Hz), 1.80 (1H, m), 4.00 (2H, d, J = 7.2 Hz), 5.14 (1H, m), 8.65−8.67 (4H, m). ^{13}C NMR (100 MHz, d_6-DMSO): 10.5 (CH_3), 13.9 (CH_3), 18.0 (CH_3), 21.9 (CH_2), 23.0 (CH_2), 26.0 (CH_2), 31.0 (CH_2), 32.7 (CH_2), 38.7 (CH), 43.3 (CH_2), 49.2 (CH), 126.0 (C), 126.1 (C), 126.2 (C), 126.6 (C), 130.5 (CH), 130.6 (CH), 162.97 (C), 163.02 (C). Anal. Calcd for $2C_{27}H_{32}N_2O_4 \cdot H_2O$: C, 70.87; H, 7.27; N, 6.12. Found: C, 70.80; H, 6.91; N, 5.95. Mp: 144 °C.

3e: The reaction was performed on 0.491 mmol (150 mg) of **2a** and 0.491 mmol (64 μL) of 2-ethyl-*n*-butylamine using general procedure B. Workup: the brown residue was suspended in acetone and the suspension added slowly to vigorously stirred 1 M HCl(aq). The precipitate was filtered and washed with water and dried in vacuo to yield the product as a brown solid (131 mg, 69%). ^{1}H NMR (400 MHz, d_6-DMSO): 0.89 (6H, t, J = 7.3 Hz), 1.34 (4H, m), 1.81 (1H, m), 3.20 (1H, t, J = 2.4 Hz), 4.01 (2H, d, J = 7.2 Hz), 4.82 (2H, d, J = 2.4 Hz), 8.68−8.74 (4H, m). ^{13}C NMR (100 MHz, d_6-DMSO): 10.5 (CH_3), 22.9 (CH_2), 29.0 (CH_2), 29.5 (CH_2), 31.0 (CH_2), 32.8 (CH_2), 38.8 (CH), 49.3 (CH), 73.5 (CH), 78.8 (C), 125.6 (C), 126.0 (C), 126.2 (C), 126.9 (C), 130.5 (CH), 130.8 (CH), 161.9 (C), 162.9 (C). Anal. Calcd for $4C_{27}H_{32}N_2O_4 \cdot H_2O \cdot (CH_3)_2CO$: C, 70.01; H, 5.44; N, 6.88. Found: C, 69.74; H, 5.11; N, 6.62. Mp: 235 °C.

3f: The reaction was performed on 0.285 mmol (100 mg) of **2b** and 0.285 mmol (103 mg) of H-L-Cys(Trt)-OH using general procedure B. Workup: the brown residue was suspended in acetone and the suspension added slowly to vigorously stirred 1 M HCl(aq). The precipitate was filtered and washed with water and dried in vacuo to yield the product as a yellow solid (120 mg, 61%). ^{1}H NMR (400 MHz, d_6-DMSO): 0.89 (6H, t, J = 7.3 Hz), 1.34 (4H, m), 1.81 (1H, m), 3.11 (2H, dd, J_1 = 4.5 Hz, J_2 = 13.0 Hz), 4.01 (2H, d, J = 7.2 Hz), 5.55 (1H, dd, J_1 = 4.3 Hz, J_2 = 10.5 Hz), 7.17−7.22 (15H, m), 8.68−8.74 (4H, m). ^{13}C NMR (100 MHz, d_6-DMSO): 10.5 (CH_3), 22.9 (CH_2), 30.3 (CH_2), 38.8 (CH), 43.4 (CH_2), 52.1 (CH), 66.5 (C), 125.0 (C), 126.5 (C), 126.8 (CH), 127.1 (C), 128.0 (CH), 128.4 (C), 129.0 (CH), 130.6 (CH), 131.5 (CH), 144.0 (C), 162.0 (C), 163.0 (C), 169.2 (C). Anal. Calcd for $2C_{42}H_{36}N_2O_6S \cdot H_2O$: C, 71.47; H, 5.28; N, 3.97. Found: C, 71.18; H, 5.09; N, 3.87. Mp: 156 °C.

3g: The reaction was performed on 0.327 mmol (100 mg) of **2a** and 0.327 mmol (119 mg) of H-L-Cys(Trt)-OH using general procedure B. Workup: the brown residue was suspended in acetone and the suspension added slowly to vigorously stirred 1 M HCl(aq). The precipitate was filtered and washed with water and dried in vacuo to yield the product as a yellow solid (156 mg, 73%). ^{1}H NMR (400 MHz, d_6-DMSO): 3.21 (1H, m), 4.82 (2H, m), 5.55 (1H, dd, J_1 = 4.3 Hz, J_2 = 10.3 Hz), 7.19−7.23 (15H, m), 8.73 (2H, d, J = 7.6 Hz), 8.75 (2H, d, J = 7.6 Hz), 13.15 (1H, s). ^{13}C NMR (100 MHz, d_6-DMSO): 29.5 (CH_2), 30.3 (CH_2), 52.3 (CH), 66.5 (C), 73.5 (CH), 78.9 (C), 125.3 (C), 125.8 (C), 126.3 (C), 126.76 (C), 126.82 (CH), 128.0 (CH), 129.0 (CH), 130.8 (CH), 131.5 (CH), 144.0 (C), 161.90 (C), 161.92 (C), 169.2 (C). Anal. Calcd for $3C_{39}H_{26}N_2O_6S \cdot 4H_2O$: C, 69.42; H, 4.28; N, 4.15. Found: C, 69.28; H, 4.03; N, 3.90. Mp: 194 °C.

3h: The reaction was performed on 0.285 mmol (100 mg) of **2b** and 0.285 mmol (37 mg) of H-L-Ile-OH using general procedure B. Workup: the brown residue was suspended in acetone and the suspension added slowly to vigorously stirred 1 M HCl(aq). The precipitate was filtered and washed with water and dried in vacuo to yield the product as a yellow solid (81 mg, 62%). ^{1}H NMR (400 MHz, d_6-DMSO): 0.76 (3H, t, J = 7.3 Hz), 0.89 (7H, t, J = 7.3 Hz), 1.21 (3H, d, J = 6.5 Hz), 1.34 (5H, m), 1.80 (1H, m), 4.01 (2H, d, J = 7.2 Hz), 5.22 (1H, d, J = 9.1 Hz), 8.71 (2H, d, J = 7.6 Hz), 8.74 (2H, d, J = 7.6 Hz), 12.80 (1H, s). ^{13}C NMR (100 MHz, d_6-DMSO): 10.5 (CH_3), 10.9 (CH_3), 18.0 (CH_3), 22.9 (CH_2), 24.7 (CH_2), 33.1 (CH), 38.8 (CH), 43.4 (CH_2), 57.9 (CH), 125.1 (C), 126.2 (C), 126.4 (C), 126.9 (C), 130.7 (CH), 131.4 (CH), 162.6 (C), 162.9

(C), 170.2 (C). Anal. Calcd for $2C_{26}H_{28}N_2O_6 \cdot H_2O$: C, 65.95; H, 6.17; N, 5.92. Found: C, 65.66; H, 5.86; N, 5.72. Mp: 135 °C.

3i: The reaction was performed on 0.285 mmol (100 mg) of **2b** and 0.285 mmol (58 mg) of H-L-Trp-OH using general procedure B. Workup: the brown residue was suspended in acetone and the suspension added slowly to vigorously stirred 1 M HCl(aq). The precipitate was filtered and washed with water and dried in vacuo to yield the product as a brown-red solid (123 mg, 82%). ^{1}H NMR (400 MHz, d_6-DMSO): 0.88 (6H, t, J = 7.1 Hz), 1.32 (4H, m), 1.79 (1H, m), 4.00 (2H, d, J = 7.1 Hz), 5.90 (1H, dd, J_1 = 5.5 Hz, J_2 = 9.4 Hz), 6.82 (1H, t, J = 7.7 Hz), 6.93 (1H, t, J = 7.7 Hz), 7.04 (1H, d, J = 2.2 Hz), 7.19 (1H, d, J = 8.1 Hz), 7.48 (1H, d, J = 8.1 Hz), 8.64 (4H, m), 10.64 (1H, s). ^{13}C NMR (100 MHz, d_6-DMSO): 10.5 (CH_3), 22.9 (CH_2), 24.0 (CH_2), 38.7 (CH), 43.4 (CH_2), 54.2 (CH), 110.6 (C), 111.3 (CH), 118.0 (CH), 118.3 (CH), 120.8 (CH), 123.6 (CH), 125.2 (C), 125.9 (C), 126.2 (C), 126.8 (C), 127.1 (C), 130.5 (CH), 131.1 (CH), 135.9 (C), 162.2 (C), 162.9 (C), 170.6 (C). Anal. Calcd for $C_{31}H_{27}N_3O_6 \cdot H_2O$: C, 67.02; H, 5.26; N, 7.56. Found: C, 66.75; H, 4.89; N, 7.66. Mp: 178 °C.

3j: The reaction was performed on 1.423 mmol (500 mg) of **2b** and 1.423 mmol (312 mg) of 4-iodoaniline using general procedure B. Workup: the brown residue was suspended in acetone and the suspension added slowly to vigorously stirred 1 M HCl(aq). The precipitate was filtered and washed with water and dried in vacuo to yield the product as a pale brown solid (300 mg, 38%). ^{1}H NMR (400 MHz, d_6-DMSO): 0.90 (6H, t, J = 7.3 Hz), 1.33 (4H, m), 1.81 (1H, m), 4.03 (2H, d, J = 7.2 Hz), 7.26 (2H, d, J = 8.6 Hz), 7.93 (2H, d, J = 8.6 Hz), 8.69 (2H, d, J = 7.6 Hz), 8.70 (2H, d, J = 7.6 Hz). ^{13}C NMR (100 MHz, d_6-DMSO): 10.5 (CH_3), 23.0 (CH_2), 38.7 (CH), 43.5 (CH_2), 123.7 (C), 126.8 (C), 127.0 (C), 128.5 (C), 130.5 (CH), 131.4 (CH), 131.8 (CH), 135.5 (C), 137.9 (CH), 159.7 (C), 162.8 (C), 163.0 (C). Anal. Calcd for $C_{26}H_{21}IN_2O_4 \cdot H_2O$: C, 54.75; H, 4.06; N, 4.91. Found: C, 54.76; H, 3.86; N, 4.79. Mp: 261 °C dec.

3k: The reaction was performed on 1.423 mmol (500 mg) of **2b** and 1.423 mmol (167 mg) of 4-ethynylaniline using general procedure B. Workup: the brown residue was suspended in acetone and the suspension added slowly to vigorously stirred 1 M HCl(aq). The precipitate was filtered and washed with water and dried in vacuo to yield the product as a pale brown solid (212 mg, 33%). ^{1}H NMR (400 MHz, d_6-DMSO): 0.90 (6H, t, J = 7.3 Hz), 1.35 (4H, m), 1.82 (1H, m), 4.03 (2H, d, J = 7.2 Hz), 4.31 (1H, s), 7.76 (2H, d, J = 8.4 Hz), 7.67 (2H, d, J = 8.4 Hz), 8.69 (2H, d, J = 7.8 Hz), 8.70 (2H, d, J = 7.8 Hz). ^{13}C NMR (100 MHz, d_6-DMSO):10.5 (CH_3), 23.0 (CH_2), 38.7 (CH), 43.4 (CH_2), 81.6 (C), 82.9 (CH), 122.0 (C), 126.26 (C), 126.34 (C), 126.6 (C), 126.8 (C), 129.5 (CH), 130.4 (CH), 130.6 (CH), 132.4 (CH), 136.1 (C), 162.8 (C), 163 (C). Anal. Calcd for $2C_{28}H_{22}N_2O_4 \cdot H_2O$: C, 73.19; H, 5.05; N, 6.10. Found: C, 73.30; H, 4.92; N, 6.06. Mp: 284 °C dec.

3l: The reaction was performed on 0.163 mmol (100 mg) of **3c** and 0.163 mmol (22 μL) of 2-ethylbuytlamine using general procedure B. Yield: 93 mg, 94%. ^{1}H NMR (400 MHz, d-$CDCl_3$): 0.96−0.99 (6H, t, J = 6.4 Hz), 1.35−1.44 (4H, dt, J = 6.8 Hz, J = 12.8 Hz), 1.85−1.92 (1H, m), 3.14−3.25 (2H, m), 4.14−4.16 (2H, d, J = 7.2 Hz), 5.53−5.57 (1H, dd, J = 5.2 Hz, J = 9.6 Hz), 7.11−7.32 (15H, m), 8.70−8.76 (2H, 2d, J = 8.1 Hz). ^{13}C NMR (100 MHz, d-$CHCl_3$): 172.7 (C), 163.3 (C), 162.2 (C), 144.4 (C), 131.7 (CH), 131.2 (CH), 129.7 (CH), 128.1 (CH), 127.1 (C), 126.9 (CH), 126.2 (C), 67.6 (C), 53.0 (CH), 44.6 (CH_2), 39.7 (CH), 30.6 (CH_2), 23.7 (CH_2), 10.8 (CH_3). Mp: 120 °C dec. HRMS (ESI+) (m/z): calcd for $C_{42}H_{36}N_2O_6SNa$ $[M + Na]^+$, 719.2186; found, 719.2176.

3m: The reaction was performed on 0.163 mmol (100 mg) of **3c** and 0.163 mmol (39 mg) of H-L-Phe(4-Br)-OH using general procedure B. Yield: 123 mg, 90%. ^{1}H NMR (400 MHz, d_6-DMSO): 2.89−2.95 (1H, dd, J = 10.8 Hz, J = 13.2 Hz), 3.11−3.16 (1H, dd, J = 4.8 Hz, J = 13.2 Hz), 3.27−3.32 (1H, dd, J = 6.4 Hz, J = 11.2 Hz), 3.56−3.61 (1H, dd, J = 5.6 Hz, J = 14.0 Hz), 5.51−5.55 (1H, dd, J = 4.4 Hz, J = 10.4 Hz), 5.85−5.88 (1H, dd, J = 5.6 Hz, J = 9.2 Hz), 7.14−7.32 (20H, m), 8.69 (4H, s). ^{13}C NMR (100 MHz, d_6-DMSO): 170.1 (C), 169.2 (C), 162.1 (C), 161.8 (C), 144.0 (C), 137.3 (C), 131.5 (CH), 131.3 (CH), 131.0 (CH), 129.0 (CH), 127.9 (CH), 126.7 (CH), 126.2 (C), 125.7 (C), 125.6 (C), 119.5 (C), 66.5 (C), 54.4 (CH), 52.3 (CH), 33.6 (CH_2), 30.2 (CH_2). Mp: 196 °C dec. HRMS (ESI+) (m/z): calcd for $C_{45}H_{31}BrN_2O_8SNa$ $[M + Na]^+$, 862.6944; found, 862.6957.

3n: The reaction was performed on 0.163 mmol (100 mg) of **3c** and 0.163 mmol (21 mg) of H-L-Ile-NH_2 using general procedure B. Yield: 103 mg, 87%. ^{1}H NMR (400 MHz, d-$CDCl_3$): 0.79−0.81 (3H, t, J = 6.8 Hz), 1.04 (1H, m), 1.18−1.20 (3H, d, J = 6.8 Hz), 1.22−1.29 (1H, m), 2.70−2.78 (1H, m), 3.19−3.22 (2H, m), 5.31−5.34 (1H, d, J = 10.4 Hz), 5.52−5.56 (1H, dd, J = 6.4 Hz, J = 9.6 Hz), 7.10−7.31 (15H, m), 8.69−8.76 (4H, 2d, J = 7.6 Hz). ^{13}C NMR (100 MHz, d_6-DMSO):170.1 (C), 169.3 (C), 162.8 (C), 162.1 (C), 144.1 (C), 131.7 (CH), 130.9 (CH), 129.0 (CH) 128.1 (CH), 127.1 (C), 126.9 (CH), 126.7 (C), 126.2 (C), 125.2 (C), 66.5 (C), 55.5 (CH), 52.2 (CH), 32.6 (CH), 30.3 (CH_2), 24.6 (CH_2), 18.7 (CH_3), 11.2 (CH_3). Mp: 224 °C dec. HRMS (ESI+) (m/z): calcd for $C_{42}H_{36}N_3O_7S$ $[M + H]^+$, 726.2274; found, 726.2285.

3o: The reaction was performed on 0.163 mmol (100 mg) of **3c** and 0.163 mmol (61 mg) of H-L-Cys(Trt)-OMe·HCl using general procedure B. Yield: 141 mg, 89%. ^{1}H NMR (400 MHz, d-$CDCl_3$): 3.16−3.25 (4H, m), 3.63(3H, s), 5.47−5.51 (1H, m), 5.53−5.57(1H, m), 7.11−7.34 (30H, m), 8.68−8.72 (4H, br s). ^{13}C NMR (100 MHz, d-$CDCl_3$): 172.6 (C), 168.8 (C), 162.3 (C), 162.1 (C), 146.9 (C), 144.4 (C), 144.3 (C), 137.7 (CH), 132.6 (CH), 131.5 (CH), 130.2 (CH), 130.0 (CH), 129.7 (CH), 128.4 (CH), 128.0 (CH), 127.4 (CH), 127.0 (C), 126.9 (C), 126.8 (CH), 126.5 (C), 126.4 (C), 67.6 (C), 67.5 (C), 53.1 (CH), 52.9 (CH), 30.6 (CH_2), 30.5 (CH_2), 29.8 (CH_3). Mp: 174 °C dec. HRMS (ESI+) (m/z): calcd for $C_{59}H_{44}N_2O_8S_2Na$ $[M + Na]^+$, 995.2431; found, 995.2425.

3p: The reaction was performed on 0.163 mmol (100 mg) of **3c** and 0.163 mmol (59 mg) of H-L-Cys(Trt)-NH_2 using general procedure B. Yield: 133 mg, 85%. ^{1}H NMR (400 MHz, d_6-DMSO): 2.86−2.97 (2H, m), 3.09−3.13 (1H, dd, J = 3.2 Hz, J = 10.4 Hz), 3.17−3.21 (1H, dd, J = 4.0 Hz, J = 10.4 Hz), 5.37−5.40 (1H, dd, J = 3.2 Hz, J = 8.4 Hz), 5.56−5.89 (1H, dd, J = 3.6 Hz, J = 8.0 Hz), 7.14−7.22 (30H, m), 8.70−8.755 (4H, 2d, J = 6.4 Hz). ^{13}C NMR (100 MHz, d_6-DMSO): 169.2 (C), 168.9 (C), 162.3 (C), 161.9 (C), 144.2 (C), 144.0 (C), 131.5 (CH), 130.9 (CH), 128.9 (CH), 128.0 (CH), 127.9 (CH), 126.9 (CH), 126.8 (CH), 126.7 (CH), 126.5 (CH), 126.1 (C), 125.3 (C), 66.4 (C), 66.3 (C), 53.0 (CH), 52.2 (CH), 30.3 (CH_2), 30.1 (CH_2). Mp: 198 °C dec. HRMS (ESI+) (m/z): calcd for $C_{58}H_{43}N_3O_7S_2Na$ $[M + Na]^+$, 980.2420; found, 980.2424.

3q: The reaction was performed on 0.163 mmol (100 mg) of **3c** and 0.163 mmol (40 mg) of H-L-Lys(Boc)-OH using general procedure B. Yield: 137 mg, 87%. ^{1}H NMR (400 MHz, d-$CDCl_3$): 1.27 (9H, s), 1.50−1.33 (2H, m), 2.21 (2H, m), 2.58 (2H, m), 3.11 (2H, m), 3.30 (2H, m), 5.46 (1H, d, J = 6.1 Hz), 5.54 (1H, m), 7.0−7.21 (15H, m), 8.61−8.76 (4H, 2d, J = 7.6 Hz). ^{13}C NMR (100 MHz, d-$CDCl_3$):173.1 (C), 171.7 (C), 162.7 (C), 162.3 (C), 144.5 (C), 131.5 (CH), 129.7 (CH), 128.0 (CH), 126.8 (CH), 126.6 (C), 67.6 (C), 53.8 (CH), 53.2 (CH), 36.9 (CH_2), 31.7 (CH_2), 30.7 (CH_2), 29.8 (CH_2), 28.5 (CH_3), 23.9 (CH_2). Mp: 230 °C dec. HRMS (ESI+) (m/z): calcd for $C_{47}H_{43}N_3O_{10}SNa$ $[M + Na]^+$ (m/z) 864.2567; found, 864.2564.

3r: The reaction was performed on 0.163 mmol (100 mg) of **3e** and 0.163 mmol (21 mg) of H-L-Gly-OMe·HCl using general procedure B. Yield: 105 mg, 94%. ^{1}H NMR (400 MHz, d_6-acetone): 3.14−3.17 (1H, dd, J = 5.2 Hz, J = 11.2 Hz), 3.40−3.44 (1H, dd, J = 5.2 Hz, J = 12 Hz), 3.78(3H, s), 4.94(2H, s), 5.60−5.64 (1H, dd, J = 3.6 Hz, J = 10.4 Hz), 7.17−7.33 (15H, m), 8.78−8.85 (4H, 2d, J = 7.6 Hz). ^{13}C NMR (100 MHz, d_6-acetone): 169.2 (C), 168.4 (C), 162.7 (C), 145.0 (C), 133.5 (CH), 132.2 (CH), 130.9 (CH), 128.9 (CH), 127.7 (C), 67.1 (C), 54.6 (CH), 53.1

(CH_2), 42.6 (CH_3), 31.5 (CH_2). Mp: 168 °C dec. HRMS (ESI+) (m/z): calcd for $C_{39}H_{29}N_3O_7SNa$ $[M + Na]^+$, 706.1624; found, 706.1611.

3s: The reaction was performed on 0.160 mmol (100 mg) of **3b** and 0.160 mmol (20 mg) of H-L-Gly-OMe·HCl using general procedure B. Yield: 99 mg, 90%. ^{1}H NMR (400 MHz, *d*-$CDCl_3$): 2.94−3.00 (1H, dd, J = 6.4 Hz, J = 14.2 Hz), 3.61−3.67 (1H, dd, J = 8.4 Hz, J = 14.2 Hz), 3.81 (3H, s), 4.98 (2H, s), 6.22−6.26 (1H, t, J = 8 Hz), 6.90 (1H, s) 7.11−7.16 (15H, m), 8.70−8.77 (4H, 2d, J = 7.6 Hz). ^{13}C NMR (100 MHz, *d*-$CDCl_3$): 171.4 (C), 168.9 (C), 168.0 (C), 162.3 (C), 162.2 (C), 144.0 (C), 131.4 (CH), 131.3 (CH), 128.5 (CH), 127.8 (CH), 127.0 (CH), 126.9 (C), 126.8 (C), 126.4 (C), 126.3 (C), 70.9 (C), 52.7 (CH_3), 50.2 (CH), 41.5 (CH_2), 37.4 (CH_2). Mp: 174 °C dec. HRMS (ESI+) (m/z): calcd for $C_{40}H_{30}N_3O_9$ $[M + H]^+$, 696.1982; found, 696.1974.

3t: The reaction was performed on 0.187 mmol (100 mg) of **3n** and 0.187 mmol (25 μL) of 2-ethylbutylamine using general procedure B. Yield: 106 mg, 91%. ^{1}H NMR (400 MHz, *d*-$CDCl_3$): 0.85−0.89 (6H, t, J = 7.6 Hz), 1.26−1.37 (4H, m), 1.76−1.83 (1H, m), 3.35−3.41 (1H, dd, J = 10 Hz, J = 14.2 Hz), 3.56−3.61 (1H, dd, J = 5.6 Hz, J = 14.2 Hz), 3.701 (3H, s), 4.06−4.08 (2H, d, J = 7.2 Hz), 4.82 (2H, s), 5.89−5.93 (1H, dd, J = 5.6 Hz, J = 10 Hz), 6.63−6.65 (2H, d, J = 8.4 Hz), 6.98−7.00 (2H, d, J = 8.8 Hz), 7.19−7.23 (5H, m), 8.58−8.66 (4H, 2d, J = 7.6 Hz). ^{13}C NMR (100 MHz, *d*-$CDCl_3$): 170.1 (C), 163.5 (C), 162.8 (C), 157.9 (C), 137.2 (C), 131.7 (CH), 131.4 (CH), 130.5 (CH), 129.4 (C), 128.9 (CH), 128.3 (CH), 127.7 (CH), 127.3 (C), 127.2 (C), 126.3 (C), 115.2 (CH), 70.2 (CH_2), 55.2 (CH), 53.1 (CH_3), 44.7 (CH_2), 39.7 (CH), 34.3 (CH_2), 23.9 (CH_2), 11.0 (CH_3). Mp: 86 °C dec. HRMS (ESI+) (m/z): calcd for $C_{37}H_{35}N_2O_7$ $[M + H]^+$, 619.2444; found, 619.2442.

3u: The reaction was performed on 0.187 mmol (100 mg) of **3n** and 0.187 mmol (23 mg) of H-L-Gly-OMe·HCl using general procedure B. Yield: 105 mg, 93%. ^{1}H NMR (400 MHz, *d*-$CDCl_3$): 3.35−3.41 (1H, dd, J = 10 Hz, J = 14.2 Hz), 3.56−3.61 (1H, dd, J = 5.6 Hz, J = 14.2 Hz), 3.70 (3H, s), 3.73 (3H, s), 4.82 (2H, s), 4.89 (2H, s), 5.89−5.93 (1H, dd, J = 5.6 Hz, J = 10 Hz), 6.63−6.65 (2H, d, J = 8.4 Hz), 6.98−7.00 (2H, d, J = 8.8 Hz), 7.19−7.23 (5H, m), 8.60−8.68 (4H, 2d, J = 7.6 Hz). ^{13}C NMR (100 MHz, *d*-$CDCl_3$): 170.1 (C), 168.4 (C), 162.8 (C), 162.6 (C), 137.2 (C), 131.7 (CH), 130.5 (CH), 129.4 (C), 128.8 (CH), 128.3 (CH), 127.7 (CH), 127.3 (C), 127.2 (C), 126.7 (C), 115.2 (CH), 70.2 (CH_2), 55.3 (CH), 53.1 (CH_3), 41.9 (CH_2), 34.3 (CH_2). Mp: 84 °C dec. HRMS (ESI+) (m/z): calcd for $C_{34}H_{27}N_2O_9$ $[M + H]^+$, 607.1717; found, 607.1724.

3v: The reaction was performed on 0.187 mmol (100 mg) of **3n** and 0.187 mmol (48 mg) of H-L-Phe-OtBu·HCl using general procedure B. Yield: 116 mg, 84%. ^{1}H NMR (400 MHz, *d*-$CDCl_3$): 1.46 (9H, s), 3.39−3.47 (2H, m), 3.62−3.69 (2H, m), 3.76 (3H, s), 4.90 (2H, s), 5.91−5.99 (2H, m), 6.71−6.74 (2H, d, J = 8.4 Hz), 7.05−7.16 (8H, m), 7.27−7.31 (4H, m), 8.64 (4H, s). ^{13}C NMR (100 MHz, *d*-$CDCl_3$): 170.3 (C), 162.7 (C), 137.6 (C), 137.2 (C), 131.7 (CH), 130.5 (CH), 129.4 (CH), 128.8 (CH), 128.3 (CH), 127.8 (CH), 127.1 (CH), 126.7 (C), 126.4 (C), 119.9 (C), 115.2 (CH), 82.8 (C), 70.4 (CH_2), 56.4 (CH), 55.3 (CH), 53.1 (CH_3), 35.8 (CH_2), 34.2 (CH_2), 28.6 (CH_3). Mp: 112 °C dec. HRMS (ESI+) (m/z): calcd for $C_{44}H_{38}N_2O_9Na$ $[M + Na]^+$, 761.2475; found, 761.2468.

■ ASSOCIATED CONTENT

Supporting Information. ^{1}H and ^{13}C spectra and characterization details for all compounds, synthetic procedures, X-ray diffraction data, and CIF data. This material is available free of charge via the Internet at http://pubs.acs.org.

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