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Catalyst-Free Synthesis of Aryl Diamines via a Three-Step Reaction Process

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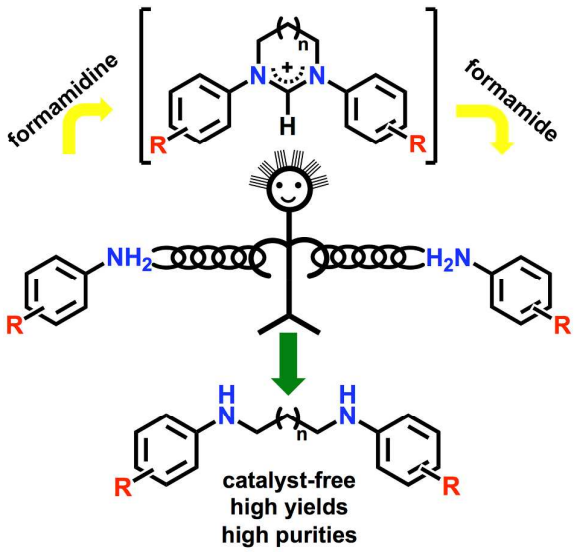


ABSTRACT: The formation of C–N bonds with aryl amines is one of the most widely studied reactions in organic chemistry. Despite this, it is still highly challenging often requiring expensive, precious metal-based catalysts. Here we report an easy catalyst-free methodology for constructing C–N bonds. The method, which proceeds via the in situ formation of closed ring amidinium ions, allows the preparation of a series of symmetrical and/or unsymmetrical aryl diamines in notably high yields (82-98 %) and purity and with a variety of different substituents. The methodology is shown successful for the preparation of aryl diamines having *para*- and/or *meta*-substituted carboxyl, nitro, bromo, methoxy, or methyl groups. This green synthetic pathway, which is catalyst free, requires only three steps, and proceeds without the need for purification. Further, it is a new sustainable, economically viable method to achieve an otherwise challenging bond formation.

INTRODUCTION

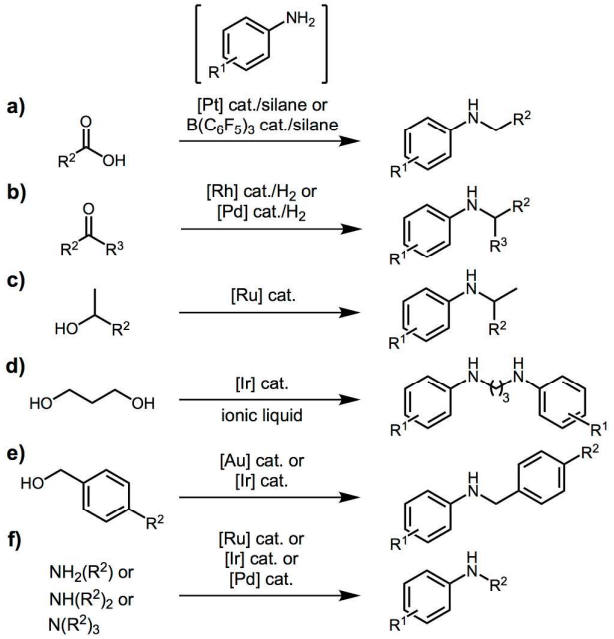
The formation of C–N bonds and N-alkylation of aryl amines are of substantial interest in synthetic chemistry due to widespread use in natural products, pharmaceuticals, bioactive compounds, conductive polymers, fine chemicals, and catalysis.[1-6] These reactions trace back to the beginning of the 20th century when Ullmann and Goldberg discovered a copper-catalyzed methodology employing aryl halides.[7-8] Much later, in the 1980s, the first Pd-catalyst was found to promote the reaction through the coupling of Sn-amides with aryl halides.[9] While the method provided moderate to good yields, the heat and moisture sensitive Sn-complexes made it unfavorable. As such, several groups began to focus on Sn-free systems; for instance, a Pd-phosphine complex was found to catalyze an intramolecular amine arylation.[10] Further, Buchwald and Hartwig developed Pd- and Cu-catalysts,[11-12] and

afterwards, reported a number of studies on C–N bond formation via substitution with alkyl/aryl halides.[4,13-16]

While the development of new ligands for catalyst systems in the past two decades has intensified research on C–N bond formation, there are still limitations.[17-21] One of the most conventional and effective approaches, carried out via nitration/reduction of arenes or reductive amination of aniline derivatives from carbonyl compounds,[22] is limited by the number of applicable substrates and has limited tolerance of functional groups. Additionally, while most recent studies allow transformation of more simple substrates, via C–H bond activation, they still require expensive metal catalysts.[23-26]

Scheme 1 summarizes selected examples of C–N bond formation using aniline-based starting materials coupled with a variety of different substrates that range from carboxylic acids (Scheme 1a),[27-28] ketones/aldehydes (Scheme 1b),[29-31] a variety of alcohols (Scheme 1c-e),[32-35] and primary, secondary, or tertiary amines (Scheme 1f).[36-39] While the majority of the aforementioned catalytic studies focus on the synthesis of alkylated/arylated monoamines, the use of appropriate substrates with relevant catalytic systems are also shown to lead to diamines (Scheme 1d).[40] In general, a survey of the literature indicates that the use of catalysts, particularly those with precious metals, appear almost unavoidable. Given the strong application-relevance of C–N coupling reactions with aryl amines, developing cheaper catalysts or catalyst-free methodologies could offer a large economic payoff.[41]

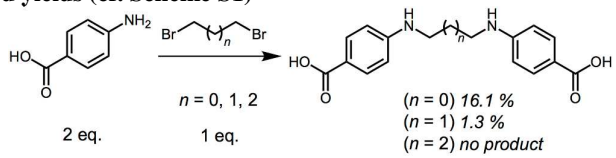
Scheme 1. Examples of reported works on N-alkylation of aniline and its derivatives using various catalysts



In this report we demonstrate a facile catalyst-free formation of C–N bonds with aryl amines, which leads to the synthesis of a series of functionalized symmetrical and unsymmetrical aryl diamine compounds with two, three or four membered alkyl chains between the amines. The reported procedure is straightforward with three easy steps and provides high product yields (82-98 %) with no need for purification. The aniline derivatives used as starting materials have varying basicities, pK_a values[42] of 1.02, 2.45, 3.29, 3.58, 3.86, 4.73 and 5.31 (for 4-Nitroaniline, 4-Aminobenzoic acid, 3-Aminobenzoic acid, 3-Bromoaniline, 4-Bromoaniline, 3-Methylaniline and 4-Methoxyaniline, respectively). This demonstrates the applicability of this method for the synthesis of a wide scope of compounds with different electron

withdrawing and donating groups (EWGs and EDGs, respectively) and at varying positions. The basicity of the substituted anilines used as starting materials exhibit pK_a's either lower or higher relative to unsubstituted aniline (pK_a value = 4.6). To date, there are a few reports showing the formation of carboxyl-substituted aryl diamines (or diimines) but with relatively low yields (33 % for *para*- and 58 % for *meta*-carboxyl). Also, due to the use of glyoxal derivatives, the reported method is limited to products containing a two-membered alkyl chain between the nitrogen atoms.[43-46] In addition to these, two earlier works report the formation of carboxyl-substituted aryl diamines; however, these methods require many steps to obtain pure materials, and the diamines are also limited to two-membered alkyl chains between the nitrogen atoms.[47-48] Some recent work also reports the synthesis of diamines using unsubstituted anilines[49-52] and substituted anilines with EDGs[50,53-55] or EWGs.[56-59] Nevertheless, these procedures have several disadvantages, such as the reactions require a catalyst, the diamine products formed are limited to two-membered alkyl chains between the nitrogen atoms (sometimes with three-membered alkyl chain), and often reactions result in very low product yields. Additionally, a procedure for the one-step synthesis of a diamine compound with two-membered alkyl chain between the nitrogen atoms and without substitutions is also reported.[60] However, our efforts applying this previously reported methodology to carboxylic acid or ester substituted anilines were unsuccessful (Scheme 2, see results and discussion for details), implying it is not successful for anilines substituted with electron withdrawing substituents. It should be noted that the presence of electron withdrawing substituents, on the aryl amines, such as -F, -CF_3 or -NO_2, -CN, -COOH(R), make direct alkylation of anilines very difficult, due to the reduced nucleophilicity of the amine.[28,31,38-39] Given that the reported work presents a new method that proceeds through an indirect way, via the in situ creation of closed ring amidinium structures, it is thought that the formation of the diamine products is still promoted despite the presence of electron-withdrawing constituents. Compounds of this kind, containing both amine and carboxyl functionality are of strong interest as building blocks for the formation of hybrid organic/inorganic materials, such as metal-organic frameworks,[43-44,46] as ligands in catalysis for aryl C–O, C–C and C–N coupling reactions,[61-66] for halogen exchange in aryl halides[67] or for hydrogenation reactions.[68-69] Last, considering drugs containing *para*-aminobenzoic acid exhibit diverse therapeutic activities, with 84 applications listed in Negwer's database,[70] C–N coupling reactions could be instrumental in the design of new pharmaceuticals.[71]

Scheme 2. Summary of attempts for one-step synthesis of diamines using dibromine based bis-electrophiles and isolated yields (cf. Scheme S1)

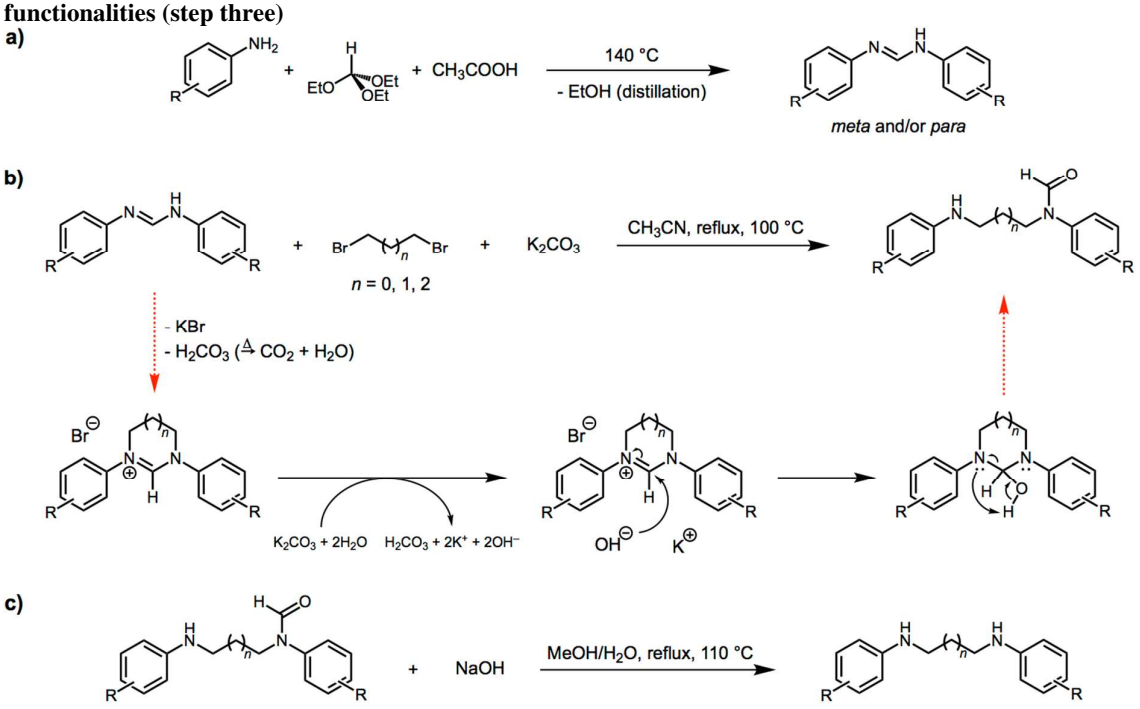


RESULTS AND DISCUSSION

In the first step, formamidine is prepared using substituted anilines with triethyl orthoformate; a similar procedure is used in previous reports but with different aniline substrates (Scheme 3a).[72-73] For the synthesis of symmetrical formamidines, the aniline derivatives (2 equiv) are mixed together with other reactants at the beginning of the reaction; however, for the synthesis of the unsymmetrical formamidine the two-different substituted anilines are added to the reaction mixture at different stages to avoid the formation of any symmetrical analogs (cross-products) that might result from side reactions. Accordingly, at the beginning of the reaction only the first substituted aniline (1 equiv) is added and allowed to reach its complete conversion to *N*-(Ethoxymethylene) aniline derivative.[74] Then, the

second substituted aniline (1 equiv) is added, and the reaction is continued under the same conditions. During the reaction, the formed ethanol is removed by distillation pushing the equilibrium in favor of the product formation. Afterwards, the formamidines are isolated as pure solids without any side products (up to 20-25 g scales) and are employed in step two without any further purification (Scheme 4). In this step, a mild base is used to deprotonate/activate the formamidine for the subsequent substitution of bromines in the dibromoalkane, and hence promotes the C–N bond formation. The use of the ester, rather than a carboxylic acid, is important to prevent the esterification[75-76] by the dibromoalkanes or polymerization.[77] The method presented in step two is previously reported for the synthesis of saturated amidinium salts with alkyl-substituted aryl groups using bases such as *n*-butyllithium or potassium carbonate (K_2CO_3).[78-80] In this case, K_2CO_3 was chosen because it does not require inert conditions or dry solvents.

Scheme 3. a) Synthetic route for the preparation of formamidines (step one), b) the in situ formation of the closed ring amidinium structures and the proposed hydrolysis mechanism leading to formamides (step two), and c) the synthesis of the aryl diamine compounds via hydrolysis of the ester and formamide functionalities (step three)

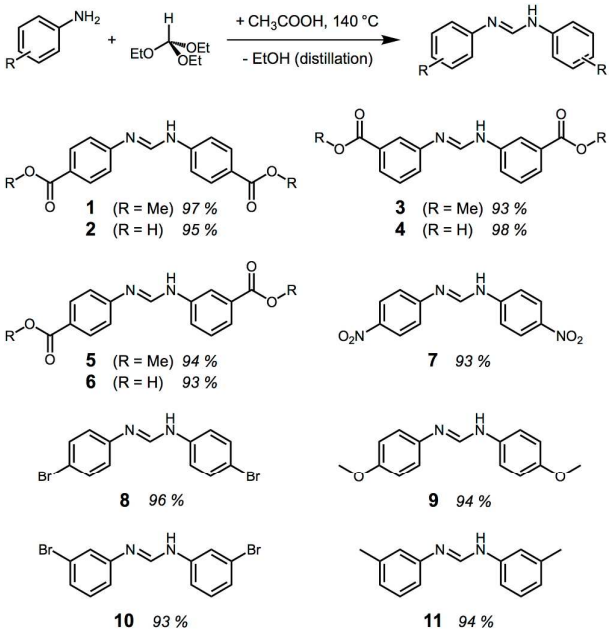


Step two (Scheme 3b) proceeds through the formation of an amidinium salt; however, relative to unsubstituted analogs or with EDGs like methyl or methoxy, the strongly EWGs such as carboxyl, nitro, or bromine decrease the electron density of the C2 carbon atom between the nitrogen atoms in the closed ring structure (EWGs also increase the acidity of the C2–H proton). As such, C2 readily undergoes nucleophilic attacks of hydroxide anions in the presence of K_2CO_3 leading to the ring opening and formation of formamides (Scheme 3b).[61] As a second scenario, following the acidity of the C2–H proton (particularly in the presence of EWGs) C2 may possibly undergo deprotonation in the presence of K_2CO_3 leading to the in situ formation of N-heterocyclic carbenes (NHCs). It is known that highly reactive, carbene species undergo hydrolysis in the presence of water subsequently leading to formamides too.[81-83] As a result of electronic effects, the reactions with the compounds containing EDGs are slower – probably due to lower reaction rates for the deprotonation of formamidines –, and need two or three times longer reaction times for completion (9a-c and 11a-c) compared

to compounds with EWGs.[80] Alternatively, the reactions with EDGs can be speeded up by using more base, such as 5 equiv K_2CO_3 instead of 3 equiv. As such, step two ends with the formation of a series of formamides (Scheme 5). While all NMR spectra taken after step two show only the formamide species, more sensitive MALDI-TOF MS analyses prove the formation of the closed ring amidinium structures in all analyzed samples from 1a, 1b and 1c (cf. Figure S1-3, *m/z* = 339.11, 353.14 and 367.17, corresponding to $C_{19}H_{19}N_2O_4^+$, $C_{20}H_{21}N_2O_4^+$ and $C_{21}H_{23}N_2O_4^+$, respectively), supporting the proposed mechanism in Scheme 3b. In an effort to eliminate hydrolysis to make the amidinium salts in higher yields, the same reactions were carried out under a nitrogen atmosphere and in dry solvents (previously dried by distillation over CaH_2 and stored in the glove box, see Experimental Section). Surprisingly, these reactions also resulted in the formation of the same formamide-based products. As such, it is hypothesized that the water stems from the thermal decomposition of carbonic acid, which is formed during the deprotonation process driven by K_2CO_3 (cf. Scheme 3b). Substituting K_2CO_3 with any other base, in the absence of water, only reveals the starting materials in the NMR spectra, implying that the in situ removal of the amidinium salt is required to drive the reaction forward towards the formamide. It should be noted, that for the purpose of synthesizing diamine compounds with alkyl chains longer than four carbon atoms between the amines, the reaction was tested with five and six membered dibromoalkanes, 1,5-dibromopentane and 1,6-dibromohexane, respectively. The reactions are found to proceed through a different mechanism as the formation of eight and nine membered ring structures (increasing strain energy) are unfavored.[84] As such, these reactions are considered to be outside the scope of this work and will be further explored in future studies.

In the final step, the formamides are easily converted into a series of aryl diamine-carboxylic acid building blocks using a standard hydrolysis procedure with sodium hydroxide (Scheme 3c). The reactions, shown in Scheme 3, provide products **1**-**35** in excellent yields, between 91 and 98 % for diamines with EWGs (carboxyl, nitro and bromine) and 82-89 % for diamines with EDGs (methyl and methoxy) (Scheme 4-6). The reason for slightly lower yields of diamines with EDGs is that these materials, **27**-**29** and **33**-**35,** remain dissolved in the water solution after neutralization and are separated via extraction using organic solvents. Even after several extractions of the aqueous reaction mixture, a small part of the products remains in the water solution, inducing slightly lower reaction yields. In contrast, the diamines with EWGs, **12**-**26** and **30**-**32,** form a suspension in water after neutralization and can be separated via filtration without the loss of the product, leading to higher reaction yields.

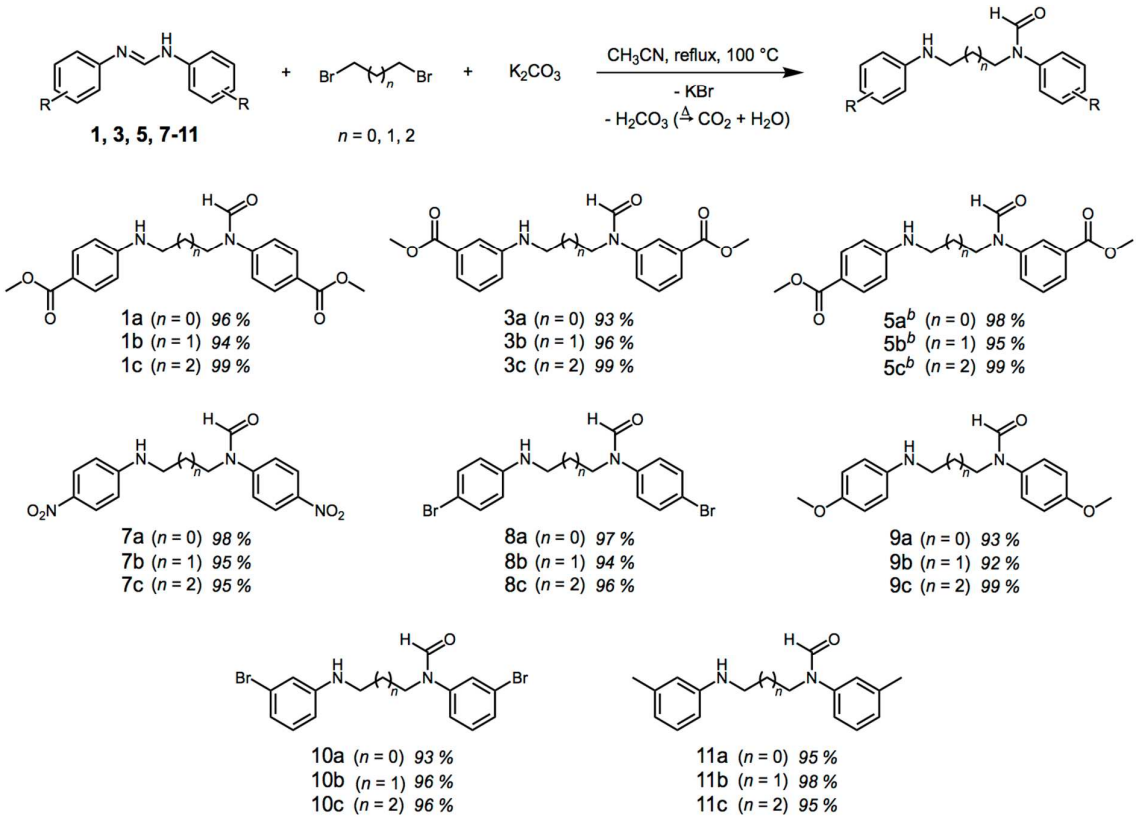
Scheme 4. Formamidines with different substituents prepared and used for the synthesis of diamine compounds[a]



[a]Reactions were carried out in a distillation apparatus at 140 °C for 24 h (without solvent), containing 2 equiv of aniline derivatives, 1.05 equiv of triethyl orthoformate, and 0.1 equiv of glacial acetic acid. All yields refer to isolated compounds.

The formamidines **1**, **3**, **5** and **7**-**11** are pure solids confirmed by NMR analysis and could directly be used for the next step. These formamidines are also quite stable; **1** shows no decomposition after 12-18 hours with heating under reflux at 100-140 °C in dimethyl formamidine, acetonitrile or tetrahydrofuran. It should be noted that **1** is partially decomposed by refluxing in methanol at 100 °C for 10 hours, and the decomposition takes place more rapidly when refluxed in a methanol/water mixture due to breakage of the imine bond. While the NMR spectra of the intermediate compounds, formamides 1a-c, 3a-c, 5a-c and 7-11a-c, show some impurities, they are still directly employed in the final hydrolysis step without any further purification (Scheme 3c). The unsymmetrical analogs of the formamides, 5a-c, are available as mixtures of two isomers where the aldehyde functionality is found either on the nitrogen atom closest to the *para*-substituted carboxylic acid (minor product) or on the nitrogen closest to the *meta*-substituted ring (major product). Products 5a and 5c both have isomer yields of 19 % and 81 %, while 5b has a slightly different distribution of 21 % and 79 %. Despite the isomeric mixtures, these products can still directly be used for the final hydrolysis in the exact same manner as the non-isomer containing reactions without any further purification (Scheme 3c).

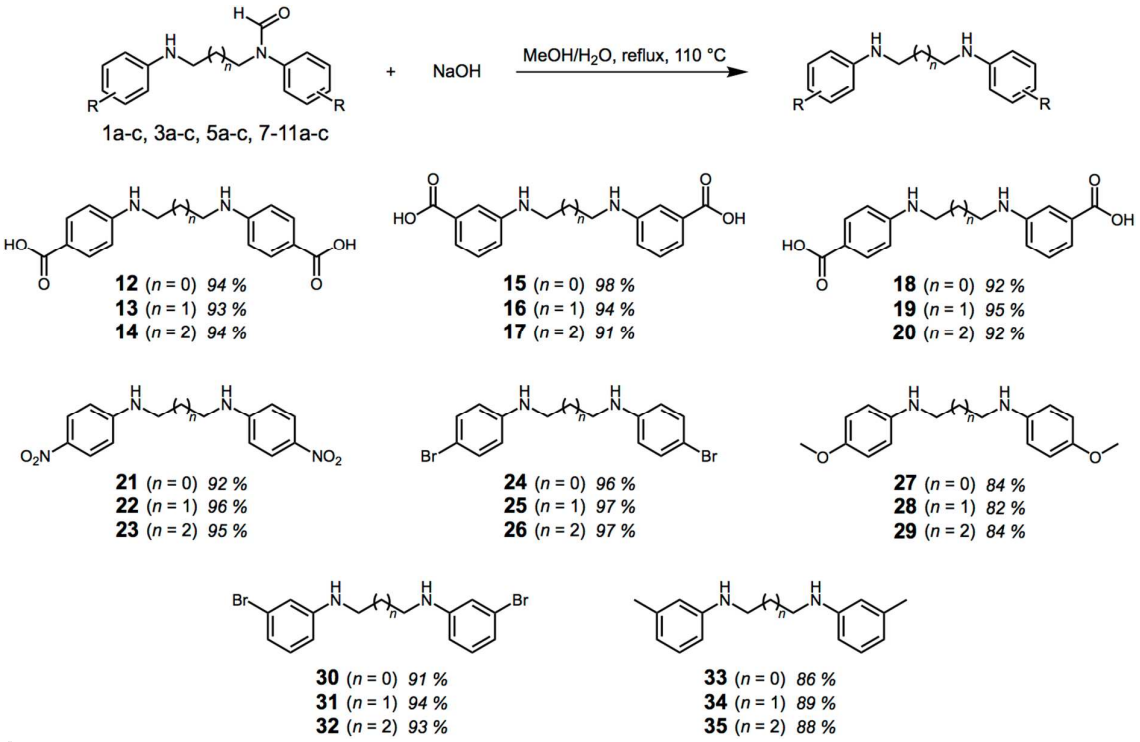
Scheme 5. The formamides obtained as intermediate compounds during the synthesis of diamine compounds[a]



[a]Reactions were refluxed in acetonitrile at 100 °C for 24-48 h (for 9a-c and 11a-c up to 5-6 days), with 1 equiv of formamidine, 1.5 equiv of dibromoalkane, and 3 equiv of potassium carbonate. [b]Several reactions result in formamides that are mixtures of two isomers, where the aldehyde functionality is located at the nitrogen atom of *para*- (minor product) or the *meta*-substituted ring (major product, shown above). The isomeric ratios are 19 and 81 % (5a, 5c) and 21 and 79 % (5b), respectively, as determined via ^{1}H NMR. All yields refer to isolated compounds.

In step three, the hydrolysis reactions result in aryl diamine compounds **12**-**35** in notable purities (Scheme 6). Due to the aforementioned water instability of the formamidines, hydrolysis of their ester forms (**1**, **3**, **5**) is carried out in acetonitrile, forming **2**, **4** and **6** (Scheme 4).

Scheme 6. Symmetrical (12-17, 21-35) and unsymmetrical (18-20) diamine compounds with different substituents synthesized in this work[a]



[a]Reactions were refluxed in a 1/2 ratio of methanol/water at 110 °C for 24 h, with 1 equiv of formamide and 10 equiv of sodium hydroxide. All yields refer to isolated compounds.

One-step synthesis. To check the possibility for direct synthesis of carboxyl or ester substituted diamines, a one-step synthesis procedure was used which has previously been reported for the synthesis of a diamine compound with two-membered alkyl chain between the nitrogen atoms and without any carboxyl-substitutions or any other EWGs.[60] As shown in Scheme 2, we tested this one-step synthesis methodology using 4-Aminobenzoic acid and dibromine based bis-electrophiles as starting materials. Even with reaction times increased to three times the reported ones, the yield for the diamine with two-membered alkyl chain was very poor (~16 %), for the diamine with three-membered alkyl chain just traces were observed (~1 %) and in the reaction with the four-membered alkyl chain no diamine formation was observed (here cyclization at the nitrogen atom of the aniline was observed, cf. Scheme S1). The same reaction with ester substituted aniline, the methyl 4-aminobenzoate, in the presence of potassium carbonate was carried out. After several days and the use of up to five equivalents of potassium carbonate, no formation of the diamine was observed. This indicates that the catalyst-free, one-step synthesis for carboxyl or ester functionalized diamine building blocks is not feasible, and hence, there is no alternative to our three-step methodology to the best of our knowledge. All details to the reactions for one-step synthesis of diamines can be found in the ESI (Scheme S1).

Thermal stability. Thermal stabilities were studied via thermogravimetric analysis (TGA); the ester forms of the formamidines (**1**, **3** and **5**) show decomposition temperatures (T_d) at ~230-240 °C, while their hydrolyzed counterparts (**2**, **4**) are less stable with decompositions under 200 °C except the unsymmetrical one (**6**), which decomposes at ~230 °C. The final diamine building blocks are in general quite stable with a very narrow one step decomposition between 195 to 275 °C. The *para*-COOH substituted analogs (**12**-**14**), with stabilities up to 274 °C, have slightly higher thermal stabilities than the *meta*-COOH substituted (**15**-**17**) and unsymmetrical diamines (**18**-**20**), 215 to 222 and 198 to 205 °C, respectively. Moreover, *para*-NO_2 (**21**-**23**) and *meta*-Br (**30**-**32**) substituted diamines exhibit

quite high decomposition temperatures at ~260-275 °C and ~240-260 °C, respectively. In contrast, *para*-Br (**24**-**26**), *para*-OMe (**27**-**29**) and *meta*-Me (**33**-**35**) substituted diamines show slightly lower stabilities with decomposition at ~195-200 °C (cf. Figure S140-169).

Single crystal X-ray analysis. Selected single crystal structures from each step of Scheme 3 – formamidine (**1**), the formamide (1a, 1c), and the diamine (**12**) – are shown in Figure S4-7.[85] Formamidine (**1**) has only one carbon atom between the two nitrogens, and the phenyl rings are slightly rotated in different planes (Figure S4). The C_3-N_1-C_1 angle is ca. 8.5 ° smaller than the C_1-N_2-C_2 angle, making the aryl ring on imine side more bent. The structure of the formamide (1a) is likely more flexible due to the -CH_2CH_2- group located between the nitrogen atoms (Figure S5). While the phenyl rings are only slightly rotated with regard to one another, they are located in different planes forming a stair-like structure that results from the presence of the aldehyde on N_1. In contrast to the asymmetric formamide, the diamine (**12**) is highly symmetric. The aryl rings are in the same plane and both carboxylic acid groups face the opposite direction making the molecule almost linear (Figure S7).

CONCLUSIONS

In conclusion, we demonstrate a catalyst-free methodology for the formation of C–N bonds starting with aryl amines; a challenging reaction that, more often than not, works with expensive catalysts, particularly those constructed with precious metals. We give evidence that the catalyst-free method proceeds indirectly, through the in situ formation of closed ring amidinium structures for the preparation of a series of *para*- and *meta*-substituted diamine compounds in high yields. This mechanism is important as the direct formation of these materials is hindered due to the electron withdrawing nature of the substituents such as -COOH, -Br or -NO_2. Moreover, the methodology reported here also works with aniline derivatives that have electron donating substituents such as -Me or -OMe, showing its applicability in the production of a wide scope of materials. Given this we envision that this method can easily be extended to form a variety of diamine compounds using more-substituted anilines with varying electron withdrawing and donating substituents. Building blocks with multiple substituents, particularly those with carboxyl and amine functionalities, are of interest in a manifold of applications that span supramolecular chemistry, catalysis, and pharmaceuticals. Using this method, we are already exploring the synthesis of various carboxylate-based diamines with and without larger alkyl bridges.

EXPERIMENTAL SECTION

General Procedures and Starting Materials. The reactions and experiments were carried out under air without using Schlenk technique, moisture-free inert conditions and dry solvents, unless stated otherwise. Acetonitrile, methanol, dichloromethane and *n*-hexane were obtained in analytical grade from commercially available sources and were used without any further purification or drying. The reactions under water free conditions were undertaken using standard vacuum and Schlenk techniques. For these reactions, acetonitrile was distilled after refluxing with CaH_2 overnight and stored in a glove box under a nitrogen atmosphere. 3-Aminobenzoic acid, 4-Aminobenzoic acid, 4-Nitroaniline, deuterated chloroform ($CDCl_3$) and 1,4-dibromobutane were obtained from Acros, triethyl orthoformate, potassium carbonate (anhydrous), deuterated dimethyl sulfoxide (dmso-d6) and 1,3-dibromopropane were obtained from ABCR, 3-Bromoaniline and 4-Bromoaniline were obtained from Fluorochem, sodium hydroxide, hydrochloric acid (37 %), magnesium sulfate (anhydrous), 3-Methylaniline, 4-Methoxyaniline and 1,2-dibromoethane were obtained from Sigma-Aldrich, sulfuric acid (95-97 %) and acetic acid (glacial) were obtained from Merck and used as they received. Solution NMR spectra were recorded in deuterated solvents on a BRUKER AV 200 or a BRUKER AVIII HD 400 spectrometer; data are given in ppm relative to 1% TMS

solution in $CDCl_3$ using the solvent signals as a secondary reference (^1H, ^{13}C). NMR spectra were recorded at room temperature (rt), if not mentioned otherwise. The Bruker Topspin software package (version 2.1 and 3.2) was used for measuring and Mestrenova NMR software (version 11.0.1) was used for processing of the spectra. IR spectra were recorded at rt on a PerkinElmer FT-IR/FIR spectrometer using a Diamond ATR cell with the PerkinElmer spectrum software package (a resolution of 4 cm^{-1} was used). Decomposition temperatures were determined from thermogravimetric analysis (TGA) experiments on a TGA Q500 device from TA Instruments in 100 µl platinum pans with an empty pan of the same type as reference. To infer the decomposition temperatures, the onset points were taken into account. Mass spectra for 1a-c were obtained using Matrix Assisted Laser Desorption Ionization-Time Of Flight Mass Spectrometry (MALDI-TOF MS) via the instrument from Microflex Bruker, in reflectron mode using positive polarity and with a sample concentration of 1 mg/mL in THF. High resolution mass spectrometry (HRMS) analysis was performed using Q Exactive HF Hybrid Quadrupole-Orbitrap mass spectrometer (Thermo Scientific, Germany) in ESI ionization mode with ionization source TriVersa NanoMate (Advion, USA) and quadrupole mass analyzer. Data collection for X-ray structure determinations were performed on a Bruker D8 Venture diffractometer with Photon 100 CMOS-detector using Mo-K_α radiation (λ = 0.71073 Å), and on multipurpose PILATUS@SNBL diffractometer with PILATUS2M detector at the Swiss-Norwegian Beam Lines at European Synchrotron Radiation Facility (λ = 0.7153 Å). Single crystals were mounted on top of a glass fiber and measured at 100–125 K. All calculations were performed using the SHELX-2014/7[86-87] software package. The structures were solved by direct methods and refined by least squares on weighted F^2 values for all reflections. All non-hydrogen atoms were assigned anisotropic displacement parameters and refined without positional constraints. Hydrogen atoms were located in the electron density difference map, assigned isotropic displacement parameters and refined without positional constraints. Complex neutral-atom scattering factors were used.

Synthesis of Methyl 4-aminobenzoate (starting material for 1 and 5).[88] 4-Aminobenzoic acid (20 g, 145.8 mmol) was suspended in 250 mL methanol in a 500 mL round-bottom flask, and concentrated sulfuric acid (95-97 %, 15 mL) were dropped in the reaction mixture by stirring within 15 min. Following the mixture was refluxed for 20 h at 100 °C and residual solvent was removed using rotary evaporator. Afterwards, the white solid was suspended in 250 mL water and by stirring saturated sodium carbonate solution was added (until pH = 3-4). Then, the mixture was filtered on a G4 frit, resulting white solid was washed with 500 mL water and dried at 60 °C in vacuum (0.1 Pa) for 12 h. Isolated yield (white powder): 19.9 g (90.3 %). ^1H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 7.85 (d, *J* = 8.6 Hz, 2H), 6.63 (d, *J* = 8.7 Hz, 2H), 4.06 (m, 2H), 3.85 (s, 3H). The data are in agreement with those reported in the literature.[88]

Synthesis of Methyl 3-aminobenzoate (starting material for 3 and 5).[88] 3-Aminobenzoic acid (20 g, 145.8 mmol) was suspended in 250 mL methanol in a 500 mL round-bottom flask, and concentrated sulfuric acid (95-97 %, 15 mL) were dropped in the reaction mixture by stirring within 15 min. Following the mixture was refluxed for 20 h at 100 °C and residual solvent was removed using rotary evaporator. Afterwards, the red-brown liquid was mixed with 250 mL water and by stirring saturated sodium carbonate solution was added (until pH = 3-4). Then, the emulsion was taken in 150 mL CH_2Cl_2 in a separation funnel, organic phase was separated and the aqueous phase was extracted with more CH_2Cl_2 (3x150 mL). Collected organic phases were dried over $MgSO_4$, the solvent was removed by rotary evaporation and resulting red-brown oil was dried at rt in vacuum (0.1 Pa) for 12 h. Isolated yield (reddish oil): 20.1 g (91.2 %). ^1H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 7.41 (d, *J* = 7.7 Hz,

1H), 7.34 (t, *J* = 2.0 Hz, 1H), 7.19 (t, *J* = 7.8 Hz, 1H), 6.84 (dd, *J* = 7.9, 1.9 Hz, 1H), 3.87 (s, 3H), 3.78 (m, 2H). The data are in agreement with those reported in the literature.[88]

Synthesis of symmetrical formamidines (1, 3, 7-11). Methyl aminobenzoate (2 equiv), triethyl orthoformate (1.05 equiv) and glacial acetic acid (0.1 equiv) were weighed in a 50 mL round bottom flask that was then connected to a distillation apparatus. The mixture was heated to 140 °C with stirring for 24 h. The formed ethanol was distilled off during reaction driving it forward. After cooling to rt, the crude solid was washed with *n*-hexane, dried in a rotary evaporator and ground in a mortar. Afterwards, the powder was taken in a G4 frit and rinsed several times with *n*-hexane. After drying at rt in vacuum (0.1 Pa) for 1 d, the product was stored in glove box.

Synthesis of unsymmetrical formamidine (5). Methyl 4-aminobenzoate (1 equiv), triethyl orthoformate (1.05 equiv) and glacial acetic acid (0.1 equiv) were weighed in a 50 mL round bottom flask that was then connected to a distillation apparatus. The mixture was heated to 140 °C with stirring for 12 h. After it methyl 3-aminobenzoate (1 equiv) was added in the reaction mixture and heated at 140 °C for 24 h. The formed ethanol was distilled off during the reaction driving it forward. After cooling to rt, the crude solid was washed with *n*-hexane, dried in a rotary evaporator and ground in a mortar. Afterwards, the powder was taken in a G4 frit and rinsed several times with *n*-hexane. After drying at rt in vacuum (0.1 Pa) for 1 d, the product was stored in glove box.

Synthesis of formamidine building blocks (2, 4, 6). The formamidine (1 equiv) and sodium hydroxide (6 equiv) were weighed in a round bottom flask. Acetonitrile (approx. 15 mL solvent/1 mmol formamidine) was added, and the mixture was refluxed at 110 °C for 48 h. After cooling to rt, acetonitrile was removed by rotary evaporation. The solid remaining in the flask was dissolved in water (approx. 10 mL solvent/1 mmol formamidine) and the clear solution was neutralized with the dropwise addition of 3 M HCl solution causing the formation of a solid. The resulting suspension was filtered over a G4 frit and the cake was washed several times with water. The product was rinsed with *n*-hexane and dried at 60 °C in vacuum (0.1 Pa) for 12 h.

Synthesis of diamine compounds (12-35). For the synthesis of diamine building blocks, firstly, the preparation of intermediate compounds, the formamides (1a-c, 3a-c, 5a-c, 7a-c, 8a-c, 9a-c, 10a-c and 11a-c) was taken place. For this purpose, the formamidine (1 equiv), dibromoalkane (1.5 equiv) and potassium carbonate (3 equiv) were weighed in a round bottom flask. Acetonitrile (approx. 15 mL solvent/1 mmol formamidine) was added and the mixture was refluxed at 100 °C for 24-48 h (for 9a-c and 11a-c the reflux time was longer, up to 5-6 days). For selected reactions, NMR was used to watch the reaction proceed, and more dibromoalkane was added (0.5-1 equiv) when needed. After complete conversion to the formamide, as observed by NMR, the mixture was cooled to rt and acetonitrile was removed using a rotary evaporator. The remaining solid was dissolved in dichloromethane and filtered over a G4 frit (because nitro-substituted formamides (7a-c) are less soluble in dichloromethane, ethanol was added during filtration to dissolve them completely). The solvent was removed by rotary evaporation; the product was rinsed with *n*-hexane and dried at rt in vacuum (0.1 Pa) for 12 h. The formamides were directly used for the following final hydrolysis reaction without any further purification.

In the hydrolysis step, the formamide (1 equiv) and sodium hydroxide (10 equiv) were weighed in a round bottom flask. A 1/2 mixture of methanol/water (approx. 25 mL solvent mixture/1 mmol formamide) was added and the mixture was refluxed at 110 °C for 24 h. After cooling to rt, the clear solution was neutralized with the dropwise addition of 3 M HCl inducing the formation of a solid (for 1a-c, 2a-c, 3a-c, 7a-c, 8a-c and 10a-c) or an unclear solution without significant solid formation (9a-c and 11a-c). In the case of solid formation (1a-c, 2a-c, 3a-c, 7a-c, 8a-c and 10a-c), the resulting suspension was filtered over a G4 frit

and the cake was washed several times with water. In the other case, without solid formation (9a-c and 11a-c), the resulting unclear water solution was extracted with Et_2O and CH_2Cl_2 (with each solvent 3x). The collected organic phase was dried over $MgSO_4$, and the solvents were removed using a rotary evaporator. The products obtained in both cases were rinsed with *n*-hexane and dried at 80-100 °C in vacuum (0.1 Pa) for 1 day.

Experimental data for 1. Methyl 4-aminobenzoate (10 g, 66 mmol), triethyl orthoformate (5.15 g, 34.7 mmol), glacial acetic acid (0.2 g. 3.3 mmol); isolated yield (white powder): 10.05 g (97.3 %). ^{1}H NMR (200.13 MHz, DMSO-d_6, 298 K): δ = 10.38 (s, 1H), 8.44 (s, 1H), 7.89 (d, *J* = 8.3 Hz, 4H), 7.38 (m, 4H), 3.82 (s, 6H). ^{13}C NMR (50.32 MHz, DMSO-d_6, 298 K) δ = 166, 148.9, 130.5, 123.5, 118.8, 51.8. IR (diamond ATR): $\tilde{\nu}$ = 410 (w), 444 (w), 469 (w), 501 (m), 510 (m), 570 (m), 623 (m), 638 (m), 688 (m), 697 (s), 707 (m), 765 (vs), 775 (s), 798 (m), 819 (m), 849 (s), 912 (m), 965 (m), 994 (m), 1012 (m), 1101 (s), 1120 (s), 1168 (vs), 1181 (s), 1193 (m), 1208 (s), 1267 (vs), 1303 (s), 1327 (m), 1415 (m), 1436 (s), 1460 (w), 1488 (m), 1506 (m), 1526 (m), 1583 (s), 1595 (s), 1660 (s), 1708 (s), 2952 (w), 3001 (w), 3066 (w). T_d (TGA) = 238.8 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{17}N_2O_4^+$, 313.1183 found, 313.1173.

Experimental data for 2. Formamidine **1** (2 g, 6.4 mmol), sodium hydroxide (1.54 g, 38.4 mmol); isolated yield (yellow powder): 1.72 g (94.5 %). ^{1}H NMR (200.13 MHz, DMSO-d_6, 298 K): δ = 11.68 (s, 2H), 8.42 (s, 1H), 7.87 (d, *J* = 8.3 Hz, 4H), 7.35 (d, *J* = 8.4 Hz, 4H). ^{13}C NMR (50.32 MHz, DMSO-d_6, 298 K): δ = 167.2, 148.8, 130.7, 124.7, 118.6. IR (diamond ATR): $\tilde{\nu}$ = 420 (m), 453 (m), 505 (m), 529 (w), 565 (m), 619 (m), 638 (m), 693 (s), 767 (vs), 780 (vs), 809 (m), 845 (s), 860 (vs), 897 (m), 979 (w), 1013 (m), 1060 (s), 1118 (vs), 1185 (vs), 1221 (vs), 1257 (vs), 1324 (vs), 1353 (vs), 1434 (m), 1528 (s), 1588 (vs), 1601 (vs), 1652 (s), 1694 (vs), 2603 (m), 3078 (w), 3214 (w), 3350 (m), 3526 (w), , 3611 (w). T_d (TGA) = 163.2/234.6 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{15}H_{13}N_2O_4^+$, 285.0870; found, 285.0865.

Experimental data for 3. Methyl 3-aminobenzoate (10 g, 66 mmol), triethyl orthoformate (5.15 g, 34.7 mmol), glacial acetic acid (0.2 g. 3.3 mmol); isolated yield (white powder): 9.65 g (93.4 %). ^{1}H NMR (200.13 MHz, DMSO-d_6, 298 K): δ = 10.11 (s, 1H), 8.28 (s, 1H), 7.84 (s, 2H), 7.73 – 7.34 (m, 6H), 3.85 (s, 6H). ^{13}C NMR (50.32 MHz, DMSO-d_6, 298 K): δ = 166.3, 148.7, 130.5, 129.4, 123.1, 119.7, 52.1. IR (diamond ATR): $\tilde{\nu}$ = 417 (m), 475 (w), 547 (s), 611 (m), 669 (m), 678 (vs), 691 (m), 706 (vs), 750 (vs), 794 (m), 821 (m), 835 (w), 886 (s), 897 (s), 940 (w), 977 (s), 1007 (vs), 1028 (w), 1076 (vs), 1105 (vs), 1112 (vs), 1157 (m), 1206 (vs), 1220 (vs), 1257 (vs), 1271 (vs), 1294 (vs), 1328 (vs), 1394 (w), 1438 (s), 1447 (s), 1474 (vs), 1516 (m), 1587 (vs), 1671 (vs), 1716 (vs), 1728 (vs), 2850 (w), 2950 (m). T_d (TGA) = 228.3 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{17}N_2O_4^+$, 313.1183; found, 313.1177.

Experimental data for 4. Formamidine **3** (2 g, 6.4 mmol), sodium hydroxide (1.54 g, 38.4 mmol); isolated yield (white powder): 1.79 g (98.3 %). ^{1}H NMR (200.13 MHz, DMSO-d_6, 298 K): δ = 11.99 (s, 2H), 8.27 (s, 1H), 7.82 (s, 2H), 7.50 (dd, *J* = 33.6, 7.6 Hz, 6H). ^{13}C NMR (50.32 MHz, DMSO-d_6, 298 K): δ = 167.4, 148.6, 131.9, 129.2, 123.3, 119.9. IR (diamond ATR): $\tilde{\nu}$ = 427 (m), 502 (m), 515 (w), 561 (w), 635 (m), 677 (vs), 752 (vs), 815 (m), 890 (m), 1075 (m), 1225 (s), 1266 (vs), 1308 (vs), 1332 (vs), 1379 (vs), 1421 (m), 1482 (m), 1516 (m), 1587 (s), 1694 (vs), 1936 (w), 2535 (m). T_d (TGA) = 238.8 °C. T_d (TGA) = 197.6/272.3 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{15}H_{13}N_2O_4^+$, 285.0870; found, 285.0867.

Experimental data for 5. Methyl 4-aminobenzoate (5 g, 33 mmol), methyl 3-aminobenzoate (5 g, 33 mmol), triethyl orthoformate (5.15 g, 34.7 mmol), glacial acetic acid (0.2 g. 3.3 mmol); isolated yield (light brown powder): 9.74 g (94.3 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 10.29 (s, 1H), 8.44 (s, 1H), 7.89 (d, *J* = 8.1 Hz, 2H), 7.63 (d, *J* = 7.2 Hz, 2H),

7.58 – 6.92 (m, 4H), 3.85 (s, 3H), 3.82 (s, 3H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K) δ = 166.3, 166.1, 149, 130.6, 129.5, 123.6, 52.2, 51.9. IR (diamond ATR): $\tilde{\nu}$ = 420 (w), 462 (w), 506 (s), 537 (m), 561 (w), 614 (m), 640 (m), 666 (w), 688 (vs), 695 (s), 754 (vs), 766 (s), 794 (m), 811 (m), 844 (s), 894 (m), 964 (m), 979 (m), 1008 (m), 1081 (vs), 1102 (vs), 1114 (vs), 1182 (vs), 1203 (vs), 1274 (vs), 1324 (s), 1377 (w), 1432 (vs), 1455 (m), 1480 (m), 1494 (s), 1525 (m), 1576 (vs), 1606 (vs), 1672 (vs), 1708 (vs), 1723 (s), 2955 (m) cm^{-1}. T_d (TGA) = 234.6 °C. HRMS (ESI) *m/z*: [M + H]$^+$ calcd for $C_{17}H_{17}N_2O_4^+$, 313.1183; found, 313.1177.

Experimental data for 6. Formamidine **5** (2 g, 6.4 mmol), sodium hydroxide (1.54 g, 38.4 mmol); isolated yield (light brown powder): 1.69 g (92.8 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 11.36 (s, 2H), 8.41 (s, 1H), 7.86 (d, *J* = 7.9 Hz, 2H), 7.61 (d, *J* = 7.5 Hz, 2H), 7.55 – 6.70 (m, 4H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K): δ = 167.6, 167.3, 148.8, 130.8, 129.2, 123.7. IR (diamond ATR): $\tilde{\nu}$ = 502 (w), 636 (w), 678 (m), 758 (m), 809 (w), 854 (w), 1113 (w), 1176 (m), 1225 (m), 1337 (m), 1377 (m), 1516 (m), 1600 (m), 1694 (m), 2604 (w) cm^{-1}. T_d (TGA) = 230.4 °C. HRMS (ESI) *m/z*: [M + H]$^+$ calcd for $C_{15}H_{13}N_2O_4^+$, 285.0870; found, 285.0871.

Experimental data for 7. 4-Nitroaniline (10 g, 72.4 mmol), triethyl orthoformate (5.63 g, 38 mmol), glacial acetic acid (0.22 g. 3.6 mmol); isolated yield (yellow powder): 9.67 g (93.3 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 10.82 (s, 1H), 8.58 (s, 1H), 8.20 (d, *J* = 9.0 Hz, 4H), 7.82 – 7.12 (m, 4H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K) δ =150, 142.3, 125.1, 121.4, 116.9. The data are in agreement with those reported in the literature.[89]

Experimental data for 8. 4-Bromoaniline (10 g, 58.1 mmol), triethyl orthoformate (4.52 g, 30.5 mmol), glacial acetic acid (0.18 g. 2.9 mmol); isolated yield (gray powder): 9.89 g (96.1 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 9.90 (s, 1H), 8.19 (s, 1H), 7.44 (d, *J* = 8.2 Hz, 4H), 7.40 – 6.81 (m, 4H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K) δ = 148.3, 131.7, 121, 114.2. The data are in agreement with those reported in the literature.[90]

Experimental data for 9. 4-Methoxyaniline (10 g, 81.2 mmol), triethyl orthoformate (6.32 g, 42.6 mmol), glacial acetic acid (0.24 g. 4.1 mmol); isolated yield (gray powder): 9.81 g (94.3 %). ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 8.04 (s, 1H), 7.52 (s, 1H), 7.00 (d, *J* = 8.7 Hz, 4H), 6.86 (d, *J* = 8.9 Hz, 4H), 3.79 (s, 6H). ^{13}C NMR (100.61 MHz, Chloroform-*d*, 298 K) δ =156.3, 149, 138.1, 120.4, 114.8, 55.7. The data are in agreement with those reported in the literature.[90]

Experimental data for 10. 3-Bromoaniline (10 g, 58.1 mmol), triethyl orthoformate (4.52 g, 30.5 mmol), glacial acetic acid (0.18 g. 2.9 mmol); isolated yield (pale yellow powder): 9.6 g (93.3 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 10.00 (s, 1H), 8.30 (s, 1H), 8.00 – 7.36 (m, 2H), 7.36 – 7.04 (m, 6H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K) δ = 148.9, 130.8, 125, 122, 121.1, 118.1. Reported without complete data set elsewhere.[91-93]

Experimental data for 11. 3-Methylaniline (10 g, 93.3 mmol), triethyl orthoformate (7.26 g, 49 mmol), glacial acetic acid (0.28 g. 4.7 mmol); isolated yield (pale yellow powder): 9.81 g (93.7 %). ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 8.20 (s, 1H), 7.59 (s, 1H), 7.20 (t, *J* = 8.1 Hz, 2H), 6.91 (d, *J* = 7.7 Hz, 2H), 6.89 – 6.81 (m, 4H), 2.33 (s, 6H). ^{13}C NMR (100.61 MHz, Chloroform-*d*, 298 K) δ = 148.7, 144.5, 139.5, 129.4, 124.6, 119.9, 116, 21.6. The data are in agreement with those reported in the literature.[90]

Experimental data for 1a**.** Formamidine **1** (3 g, 9.6 mmol), 1,2-dibromoethane (2.71 g, 14.4 mmol), potassium carbonate (3.98 g, 28.8 mmol); isolated yield (yellow powder): 3.28 g (95.8 %). ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 8.52 (s, 1H), 8.06 (d, *J* = 8.7 Hz, 2H), 7.82 (d, *J* = 8.8 Hz, 2H), 7.20 (d, *J* = 8.6 Hz, 2H), 6.49 (d, *J* = 8.8 Hz, 2H), 4.57 (s, 1H), 4.12 (t, *J* = 6.0 Hz, 2H), 3.92 (s, 3H), 3.83 (s, 3H), 3.42 (t, *J* = 6.1 Hz, 2H). ^{13}C NMR (100.61 MHz, Chloroform-*d*, 298 K): δ = 167.3, 166.1, 163, 151.5, 144.7, 131.7, 131.5, 128.9, 123.1, 119, 111.5, 52.5, 51.7, 44.8, 42. IR (diamond ATR): $\tilde{\nu}$ = 404 (w), 423 (vw), 457

(m), 482 (w), 498 (m), 518 (s), 584 (m), 635 (w), 694 (vs), 768 (vs), 825 (s), 840 (s), 861 (m), 956 (s), 988 (m), 1014 (s), 1034 (m), 1098 (vs), 1112 (vs), 1134 (s), 1181 (vs), 1202 (s), 1275 (vs), 1320 (m), 1347 (s), 1429 (vs), 1462 (m), 1495 (m), 1513 (m), 1537 (s), 1577 (s), 1603 (vs), 1663 (vs), 1709 (vs), 1722 (s), 1916 (w), 2899 (w), 2958 (w), 3032 (w), 3361 (m).

Experimental data for 1b**.** Formamidine **1** (3 g, 9.6 mmol), 1,3-dibromopropane (2.91 g, 14.4 mmol), potassium carbonate (3.98 g, 28.8 mmol); isolated yield (yellow powder): 3.34 g (93.9 %). ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 8.53 (s, 1H), 8.08 (d, *J* = 8.7 Hz, 2H), 7.83 (d, *J* = 8.8 Hz, 2H), 7.21 (d, *J* = 8.7 Hz, 2H), 6.53 (d, *J* = 8.8 Hz, 2H), 4.66 (s, 1H), 3.99 (t, *J* = 6.6 Hz, 2H), 3.93 (s, 3H), 3.84 (s, 3H), 3.21 (t, *J* = 6.4 Hz, 2H), 1.84 (p, *J* = 6.5 Hz, 2H). ^{13}C NMR (100.61 MHz, Chloroform-*d*, 298 K): δ = 167.4, 166.1, 162.4, 151.7, 144.6, 131.7, 131.5, 128.7, 122.7, 118.6, 111.7, 52.4, 51.6, 42, 40.1, 26.9. IR (diamond ATR): $\tilde{\nu}$ = 427 (w), 509 (m), 566 (w), 634 (w), 649 (w), 700 (s), 769 (vs), 820 (w), 843 (s), 968 (m), 991 (m), 1005 (m), 1106 (vs), 1114 (vs), 1132 (m), 1171 (vs), 1190 (s), 1265 (vs), 1280 (vs), 1312 (m), 1341 (s), 1387 (w), 1422 (m), 1434 (vs), 1477 (m), 1529 (s), 1576 (s), 1599 (vs), 1679 (vs), 1924 (vw), 2906 (w), 2952 (w), 2995 (w), 3376 (m).

Experimental data for 1c**.** Formamidine **1** (3 g, 9.6 mmol), 1,4-dibromobutane (3.11 g, 14.4 mmol), potassium carbonate (3.98 g, 28.8 mmol); isolated yield (brown powder): 3.67 g (99.4 %). ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 8.50 (s, 1H), 8.07 (d, *J* = 8.7 Hz, 2H), 7.83 (d, *J* = 8.8 Hz, 2H), 7.20 (d, *J* = 8.7 Hz, 2H), 6.51 (d, *J* = 8.8 Hz, 2H), 4.37 (s, 1H), 3.93 (s, 3H), 3.91 (t, *J* = 6.8 Hz, 2H), 3.83 (s, 3H), 3.17 (t, *J* = 6.4 Hz, 2H), 1.72 – 1.57 (m, 4H). ^{13}C NMR (100.61 MHz, Chloroform-*d*, 298 K): δ = 167.4, 166.2, 162.1, 151.8, 144.8, 131.7, 131.4, 128.5, 122.7, 118.7, 111.7, 52.4, 51.6, 44.1, 43, 26.3, 25.3. IR (diamond ATR): $\tilde{\nu}$ = 420 (m), 486 (m), 504 (s), 516 (m), 557 (s), 634 (m), 655 (m), 696 (vs), 730 (m), 766 (vs), 831 (s), 859 (s), 928 (m), 942 (m), 963 (s), 981 (m), 1010 (s), 1025 (m), 1047 (m), 1096 (vs), 1112 (vs), 1128 (vs), 1176 (vs), 1235 (vs), 1245 (vs), 1271 (vs), 1312 (s), 1346 (s), 1429 (vs), 1460 (m), 1477 (s), 1491 (s), 1515 (vs), 1527 (s), 1600 (vs), 1664 (vs), 1710 (vs), 1913 (vs), 2872 (w), 2908 (w), 2953 (m), 3001 (w), 3385 (s).

Experimental data for 3a**.** Formamidine **3** (3 g, 9.6 mmol), 1,2-dibromoethane (2.71 g, 14.4 mmol), potassium carbonate (3.98 g, 28.8 mmol); isolated yield (reddish-brown viscous oil): 3.17 g (92.6 %). ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 8.44 (s, 1H), 7.96 (dt, *J* = 7.8, 1.3 Hz, 1H), 7.84 – 7.80 (m, 1H), 7.50 – 7.43 (m, 1H), 7.37 – 7.31 (m, 2H), 7.20 – 7.13 (m, 2H), 6.72 (ddd, *J* = 8.1, 2.6, 1.0 Hz, 1H), 4.19 (s, 1H), 4.11 (t, *J* = 6.1 Hz, 2H), 3.91 (s, 3H), 3.86 (s, 3H), 3.38 (t, *J* = 6.1 Hz, 2H). ^{13}C NMR (100.61 MHz, Chloroform-*d*, 298 K): δ = 167.5, 166, 163.1, 147.8, 141.1, 132.1, 131.2, 130.1, 129.3, 128.5, 128.3, 125.2, 118.9, 117.4, 113.2, 52.6, 52.1, 45, 42.4. IR (diamond ATR): $\tilde{\nu}$ = 466 (w), 515 (w), 654 (w), 686 (vs), 710 (m), 751 (vs), 806 (w), 870 (w), 894 (w), 993 (s), 1022 (m), 1083 (vs), 1105 (vs), 1209 (vs), 1237 (vs), 1281 (vs), 1344 (s), 1435 (vs), 1490 (s), 1519 (m), 1586 (vs), 1604 (vs), 1669 (vs), 1715 (vs), 2883 (w), 2951 (w), 3378 (w).

Experimental data for 3b**.** Formamidine **3** (3 g, 9.6 mmol), 1,3-dibromopropane (2.91 g, 14.4 mmol), potassium carbonate (3.98 g, 28.8 mmol); isolated yield (reddish-brown viscous oil): 3.42 g (96.1 %). ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 8.43 (s, 1H), 7.97 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.84 (t, *J* = 2.0 Hz, 1H), 7.49 (t, *J* = 7.9 Hz, 1H), 7.37 – 7.31 (m, 2H), 7.22 (dd, *J* = 2.5, 1.6 Hz, 1H), 7.19 (t, *J* = 7.8 Hz, 1H), 6.75 (ddd, *J* = 8.1, 2.6, 1.0 Hz, 1H), 3.98 (t, *J* = 6.7 Hz, 2H), 3.93 (s, 3H), 3.87 (s, 3H), 3.19 (t, *J* = 6.4 Hz, 2H), 1.83 (p, *J* = 6.6 Hz, 2H). ^{13}C NMR (100.61 MHz, Chloroform-*d*, 298 K): δ = 167.6, 166.1, 162.6, 148, 141, 132.1, 131.2, 130.1, 129.3, 128.3, 128.2, 125, 118.6, 117.6, 113.4, 52.6, 52.1, 42.4, 40.6, 27. IR (diamond ATR): $\tilde{\nu}$ = 466 (vw), 515 (w), 549 (w), 655 (m), 686 (vs), 709 (m), 751 (vs), 809 (m), 868 (m), 894 (m), 993 (s), 1027 (m), 1082 (vs), 1106 (vs), 1191 (vs), 1238 (vs), 1283 (vs), 1435 (vs), 1490 (s), 1520 (m), 1586 (vs), 1603 (vs), 1668 (vs), 1715 (vs), 2880 (w), 2951 (w), 3376 (w).

Experimental data for 3c**.** Formamidine **3** (3 g, 9.6 mmol), 1,4-dibromobutane (3.11 g, 14.4 mmol), potassium carbonate (3.98 g, 28.8 mmol); isolated yield (reddish-brown viscous oil): 3.66 g (99.1 %). ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 8.39 (s, 1H), 7.96 (dt, *J* = 7.8, 1.3 Hz, 1H), 7.83 (t, *J* = 1.9 Hz, 1H), 7.48 (t, *J* = 7.9 Hz, 1H), 7.35 (dddd, *J* = 5.8, 4.7, 2.5, 1.2 Hz, 2H), 7.26 – 7.23 (m, 1H), 7.19 (t, *J* = 7.9 Hz, 1H), 6.79 (dd, *J* = 8.0, 1.6 Hz, 1H), 3.97 (s, 1H), 3.92 (m, 5H), 3.86 (s, 3H), 3.14 (t, *J* = 6.2 Hz, 2H), 1.64 (p, *J* = 3.5 Hz, 4H). ^{13}C NMR (50.32 MHz, Chloroform-*d*, 298 K): δ = 167.6, 166.2, 162.3, 148.1, 141.1, 132.1, 131.2, 130.1, 129.3, 128.4, 128.1, 125, 118.7, 117.5, 113.4, 52.6, 52.1, 44.5, 43.6, 26.4, 25.4. IR (diamond ATR): $\tilde{\nu}$ = 426 (vw), 509 (w), 556 (w), 654 (w), 689 (vs), 709 (m), 752 (vs), 815 (w), 865 (w), 901 (w), 1001 (m), 1018 (m), 1083 (vs), 1106 (vs), 1190 (s), 1239 (vs), 1280 (vs), 1349 (s), 1436 (vs), 1490 (m), 1522 (w), 1586 (vs), 1603 (vs), 1670 (vs), 1716 (vs), 2868 (w), 2950 (m), 3384 (w).

Experimental data for 5a**.** Formamidine **5** (3 g, 9.6 mmol), 1,2-dibromoethane (2.71 g, 14.4 mmol), potassium carbonate (3.98 g, 28.8 mmol); isolated yield (reddish-brown viscous oil): 3.34 g (97.6 %). The formamide 19 is a mixture of two isomers where the aldehyde functionality is located at the nitrogen atom of *para*- (minor product) or *meta*-substituted ring (major product) at the ratio of 19 to 81 %, respectively. Major product: ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.44 (s, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.85 – 7.81 (m, 3H), 7.48 (t, *J* = 7.9 Hz, 1H), 7.34 – 7.30 (m, 1H), 6.49 (d, *J* = 8.7 Hz, 2H), 4.12 (t, *J* = 6.0 Hz, 2H), 3.92 (s, 3H), 3.84 (s, 3H), 3.40 (q, *J* = 5.8 Hz, 2H). ^{13}C NMR (100.61 MHz, Chloroform-*d*, 298 K): δ = 167.4, 166, 163.3, 151.5, 140.9, 131.7, 131.5, 130.2, 128.6, 128.5, 125.2, 123, 111.5, 52.7, 51.7, 45, 42. IR (diamond ATR): $\tilde{\nu}$ = 418 (vw), 510 (m), 637 (w), 656 (w), 697 (vs), 754 (vs), 770 (vs), 794 (vw), 839 (m), 900 (w), 968 (m), 1016 (m), 1106 (vs), 1135 (s), 1173 (vs), 1205 (vs), 1266 (vs), 1347 (s), 1433 (vs), 1491 (m), 1529 (vs), 1585 (vs), 1602 (vs), 1667 (vs), 1707 (vs), 2950 (m), 3374 (w) cm^{-1}.

Experimental data for 5b**.** Formamidine **5** (3 g, 9.6 mmol), 1,3-dibromopropane (2.91 g, 14.4 mmol), potassium carbonate (3.98 g, 28.8 mmol); isolated yield (reddish-brown viscous oil): 3.38 g (95 %). The formamide 20 is a mixture of two isomers where the aldehyde functionality is located at the nitrogen atom of *para*- (minor product) or *meta*-substituted ring (major product) at the ratio of 21 to 79 %, respectively. Major product: ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 8.44 (s, 1H), 7.98 (d, *J* = 7.8 Hz, 1H), 7.87 – 7.80 (m, 3H), 7.50 (t, *J* = 7.9 Hz, 1H), 7.37 – 7.31 (m, 1H), 6.54 (d, *J* = 8.6 Hz, 2H), 3.98 (t, *J* = 6.5 Hz, 2H), 3.94 (s, 3H), 3.84 (s, 3H), 3.22 (t, *J* = 6.1 Hz, 2H), 1.81 (p, *J* = 6.4 Hz, 2H). ^{13}C NMR (100.61 MHz, Chloroform-*d*, 298 K): δ = 167.4, 166.1, 162.7, 151.6, 140.8, 132.1, 131.7, 130.2, 128.4, 128.3, 125, 122.7, 111.7, 52.7, 51.7, 42.2, 40, 26.6. IR (diamond ATR): $\tilde{\nu}$ = 511 (m), 572 (w), 635 (w), 654 (w), 699 (s), 756 (vs), 771 (vs), 817 (w), 838 (m), 896 (w), 967 (m), 1016 (m), 1107 (vs), 1173 (vs), 1244 (vs), 1273 (vs), 1346 (s), 1433 (vs), 1490 (m), 1529 (s), 1602 (vs), 1669 (vs), 1704 (vs), 2950 (m), 3373 (w) cm^{-1}.

Experimental data for 5c**.** Formamidine **5** (3 g, 9.6 mmol), 1,4-dibromobutane (3.11 g, 14.4 mmol), potassium carbonate (3.98 g, 28.8 mmol); isolated yield (reddish-brown viscous oil): 3.66 g (99.1 %). The formamide 21 is a mixture of two isomers where the aldehyde functionality is located at the nitrogen atom of *para*- (minor product) or *meta*-substituted ring (major product) at the ratio of 19 to 81 %, respectively. Major product: ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 8.40 (s, 1H), 7.97 (d, *J* = 7.8 Hz, 1H), 7.87 – 7.80 (m, 3H), 7.49 (t, *J* = 7.9 Hz, 1H), 7.37 – 7.31 (m, 1H), 6.51 (d, *J* = 8.5 Hz, 2H), 3.95 – 3.91 (m, 5H), 3.84 (s, 3H), 3.21 – 3.13 (m, 2H), 1.66 – 1.60 (m, 4H). ^{13}C NMR (100.61 MHz, Chloroform-*d*, 298 K): δ = 167.4, 166.2, 162.4, 141, 132, 131.7, 131.4, 130.1, 128.4, 128.1, 125, 122.6, 111.6, 52.6, 51.7, 44.4, 43, 26.2, 25.3. IR (diamond ATR): $\tilde{\nu}$ = 509 (m), 581 (w), 635 (w), 653 (w), 695 (s), 757 (vs), 771 (vs), 838 (m), 966 (m), 1016 (m), 1106 (vs), 1172 (vs), 1243

(vs), 1272 (vs), 1346 (s), 1433 (vs), 1489 (m), 1530 (s), 1602 (vs), 1671 (vs), 1704 (vs), 2949 (m), 3347 (w) cm^{-1}.

Experimental data for 7a**.** Formamidine **7** (3 g, 10.5 mmol), 1,2-dibromoethane (2.95 g, 15.7 mmol), potassium carbonate (4.35 g, 31.4 mmol); isolated yield (yellow powder): 3.38 g (97.6 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 8.75 (s, 1H), 8.23 (d, *J* = 9.1 Hz, 2H), 7.96 (d, *J* = 9.0 Hz, 2H), 7.60 (d, *J* = 9.1 Hz, 2H), 7.27 (t, *J* = 6.2 Hz, 1H), 6.60 (d, *J* = 9.1 Hz, 2H), 4.04 (t, *J* = 6.7 Hz, 2H), 3.41 – 3.39 (m, 2H).

Experimental data for 7b**.** Formamidine **7** (3 g, 10.5 mmol), 1,3-dibromopropane (3.17 g, 15.7 mmol), potassium carbonate (4.35 g, 31.4 mmol); isolated yield (yellow powder): 3.41 g (94.5 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 8.74 (s, 1H), 8.24 (d, *J* = 9.2 Hz, 2H), 7.95 (d, *J* = 9.1 Hz, 2H), 7.66 (d, *J* = 9.2 Hz, 2H), 7.22 (t, *J* = 5.6 Hz, 1H), 6.56 (d, *J* = 9.3 Hz, 2H), 4.00 (t, *J* = 7.1 Hz, 2H), 3.15 – 3.10 (m, 2H), 1.78 (p, *J* = 7.1 Hz, 2H).

Experimental data for 7c**.** Formamidine **7** (3 g, 10.5 mmol), 1,4-dibromobutane (3.39 g, 15.7 mmol), potassium carbonate (4.35 g, 31.4 mmol); isolated yield (yellow powder): 3.56 g (94.8 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 8.74 (s, 1H), 8.24 (d, *J* = 9.1 Hz, 2H), 7.96 (d, *J* = 9.0 Hz, 2H), 7.64 (d, *J* = 9.2 Hz, 2H), 7.25 (t, *J* = 5.4 Hz, 1H), 6.58 (d, *J* = 9.3 Hz, 2H), 3.93 (t, *J* = 6.5 Hz, 2H), 3.12 (q, *J* = 6.1 Hz, 2H), 1.59 – 1.50 (m, 4H).

Experimental data for 8a**.** Formamidine **8** (3 g, 8.5 mmol), 1,2-dibromoethane (2.39 g, 12.7 mmol), potassium carbonate (3.51 g, 25.4 mmol); isolated yield (gray powder): 3.28 g (97.2 %). ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 8.37 (s, 1H), 7.53 (d, *J* = 8.7 Hz, 2H), 7.22 (d, *J* = 8.8 Hz, 2H), 7.03 (d, *J* = 8.7 Hz, 2H), 6.42 (d, *J* = 8.8 Hz, 2H), 4.02 (t, *J* = 6.1 Hz, 2H), 3.29 (t, *J* = 6.1 Hz, 2H).

Experimental data for 8b**.** Formamidine **8** (3 g, 8.5 mmol), 1,3-dibromopropane (2.57 g, 12.7 mmol), potassium carbonate (3.51 g, 25.4 mmol); isolated yield (pale green powder): 3.29 g (94.2 %). ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 8.36 (s, 1H), 7.54 (d, *J* = 8.7 Hz, 2H), 7.25 (d, *J* = 8.9 Hz, 3H), 7.02 (d, *J* = 8.7 Hz, 2H), 6.52 (d, *J* = 8.8 Hz, 2H), 3.91 (t, *J* = 6.6 Hz, 2H), 3.12 (t, *J* = 6.5 Hz, 2H), 1.82 (p, *J* = 6.5 Hz, 2H).

Experimental data for 8c**.** Formamidine **8** (3 g, 8.5 mmol), 1,4-dibromobutane (2.74 g, 12.7 mmol), potassium carbonate (3.51 g, 25.4 mmol); isolated yield (gray powder): 3.46 g (95.8 %). ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 8.27 (s, 1H), 7.83 – 7.69 (m, 4H), 7.52 (d, *J* = 8.6 Hz, 2H), 7.02 (d, *J* = 8.7 Hz, 2H), 4.79 – 4.63 (m, 2H), 3.75 (t, *J* = 6.7 Hz, 2H), 1.56 (p, *J* = 7.0 Hz, 2H), 1.37 (p, *J* = 7.1 Hz, 2H).

Experimental data for 9a**.** Formamidine **9** (3 g, 11.7 mmol), 1,2-dibromoethane (3.30 g, 17.6 mmol), potassium carbonate (4.85 g, 35.1 mmol); isolated yield (pale green powder): 3.28 g (93.3 %). ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 8.30 (s, 1H), 7.09 (d, *J* = 8.9 Hz, 2H), 6.91 (d, *J* = 8.9 Hz, 2H), 6.75 (d, *J* = 8.9 Hz, 2H), 6.52 (d, *J* = 8.9 Hz, 2H), 3.98 (t, *J* = 6.2 Hz, 2H), 3.82 (s, 3H), 3.73 (s, 3H), 3.26 (t, *J* = 6.2 Hz, 2H).

Experimental data for 9b**.** Formamidine **9** (3 g, 11.7 mmol), 1,3-dibromopropane (3.54 g, 17.6 mmol), potassium carbonate (4.85 g, 35.1 mmol); isolated yield (green oil): 3.39 g (92.1 %). ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 8.28 (s, 1H), 7.09 (d, *J* = 8.8 Hz, 2H), 7.03 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 9.0 Hz, 2H), 6.75 (d, *J* = 8.6 Hz, 2H), 3.89 – 3.82 (m, 5H), 3.74 (s, 3H), 3.23 – 3.15 (m, 2H), 1.79 (p, *J* = 7.5, 7.0 Hz, 2H).

Experimental data for 9c**.** Formamidine **9** (3 g, 11.7 mmol), 1,4-dibromobutane (3.79 g, 17.6 mmol), potassium carbonate (4.85 g, 35.1 mmol); isolated yield (green sticky oil): 3.82 g (99.4 %). ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 8.14 (s, 1H), 7.74 (d, *J* = 9.3 Hz, 2H), 7.02 (d, *J* = 9.3 Hz, 2H), 6.97 (d, *J* = 8.9 Hz, 2H), 6.86 (d, *J* = 8.9 Hz, 2H), 4.57 (dt, *J* = 12.5, 6.5 Hz, 2H), 3.83 (s, 3H), 3.78 (s, 3H), 3.65 (t, *J* = 6.7 Hz, 2H), 1.48 (p, *J* = 7.0 Hz, 2H), 1.35 (dt, *J* = 15.2, 7.4 Hz, 2H).

Experimental data for 10a**.** Formamidine **10** (3 g, 8.5 mmol), 1,2-dibromoethane (2.39 g, 12.7 mmol), potassium carbonate (3.51 g, 25.4 mmol); isolated yield (pale brown powder):

3.13 g (92.8 %). ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 8.40 (s, 1H), 7.46 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.32 (t, *J* = 2.0 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.08 (dd, *J* = 8.0, 2.1 Hz, 1H), 6.99 (t, *J* = 8.1 Hz, 1H), 6.80 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.65 (t, *J* = 2.1 Hz, 1H), 6.46 (dd, *J* = 8.2, 2.3 Hz, 1H), 4.04 (t, *J* = 6.1 Hz, 2H), 3.31 (q, *J* = 5.8 Hz, 2H).

Experimental data for 10b**.** Formamidine **10** (3 g, 8.5 mmol), 1,3-dibromopropane (2.57 g, 12.7 mmol), potassium carbonate (3.51 g, 25.4 mmol); isolated yield (pale green oil): 3.34 g (95.6 %). ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 8.39 (s, 1H), 7.45 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.34 – 7.30 (m, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.09 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.01 (t, *J* = 8.0 Hz, 1H), 6.82 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.75 (t, *J* = 2.1 Hz, 1H), 6.54 (dd, *J* = 8.2, 2.3 Hz, 1H), 3.92 (t, *J* = 6.6 Hz, 2H), 3.14 (t, *J* = 6.4 Hz, 2H), 1.83 (p, *J* = 6.5 Hz, 2H).

Experimental data for 10c**.** Formamidine **10** (3 g, 8.5 mmol), 1,4-dibromobutane (2.74 g, 12.7 mmol), potassium carbonate (3.51 g, 25.4 mmol); isolated yield (pale green oil): 3.47 g (96.1 %). ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 8.37 (s, 1H), 7.47 – 7.42 (m, 1H), 7.33 (t, *J* = 2.0 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.09 (dd, *J* = 8.0, 2.1 Hz, 1H), 7.00 (t, *J* = 8.0 Hz, 1H), 6.81 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.73 (t, *J* = 2.1 Hz, 1H), 6.52 (dd, *J* = 8.1, 2.3 Hz, 1H), 3.85 (t, *J* = 6.7 Hz, 2H), 3.18 – 3.02 (m, 2H), 1.69 – 1.57 (m, 4H).

Experimental data for 11a**.** Formamidine **11** (3 g, 13.4 mmol), 1,2-dibromoethane (3.77 g, 20.1 mmol), potassium carbonate (5.55 g, 40.1 mmol); isolated yield (orange oil): 3.41 g (95 %). ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 8.40 (s, 1H), 7.29 (t, *J* = 7.9 Hz, 1H), 7.13 (d, *J* = 7.6 Hz, 1H), 7.07 – 7.02 (m, 1H), 7.00 – 6.95 (m, 2H), 6.52 (d, *J* = 7.0 Hz, 1H), 6.37 (dd, *J* = 6.5, 2.4 Hz, 2H), 4.05 (t, *J* = 6.2 Hz, 2H), 3.33 (t, *J* = 6.2 Hz, 2H), 2.36 (s, 3H), 2.25 (s, 3H).

Experimental data for 11b**.** Formamidine **11** (3 g, 13.4 mmol), 1,3-dibromopropane (4.05 g, 20.1 mmol), potassium carbonate (5.55 g, 40.1 mmol); isolated yield (orange oil): 3.71 g (98.2 %). ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 8.38 (s, 1H), 7.32 – 7.27 (m, 1H), 7.12 (d, *J* = 7.8 Hz, 1H), 7.05 (t, *J* = 7.7 Hz, 1H), 7.01 – 6.93 (m, 2H), 6.53 (d, *J* = 7.7 Hz, 1H), 6.50 – 6.37 (m, 2H), 3.93 (t, *J* = 6.7 Hz, 2H), 3.15 (t, *J* = 6.5 Hz, 2H), 2.37 (s, 3H), 2.26 (s, 3H), 1.83 (p, *J* = 6.5 Hz, 2H).

Experimental data for 11c**.** Formamidine **11** (3 g, 13.4 mmol), 1,4-dibromobutane (4.33 g, 20.1 mmol), potassium carbonate (5.55 g, 40.1 mmol); isolated yield (orange oil): 3.77 g (95.1 %). ^{1}H NMR (400.13 MHz, Chloroform-*d*, 298 K): δ = 8.21 (s, 1H), 7.33 – 7.29 (m, 2H), 7.08 (t, *J* = 6.8 Hz, 2H), 7.01 – 6.94 (m, 2H), 6.80 (dd, *J* = 11.1, 3.6 Hz, 2H), 3.78 (t, *J* = 7.4 Hz, 2H), 3.33 – 3.18 (m, 2H), 2.47 (s, 3H), 2.34 (s, 3H), 1.49 (p, *J* = 6.9 Hz, 4H).

Experimental data for 12. Formamide 1a (2 g, 5.6 mmol), sodium hydroxide (2.25 g, 56 mmol); isolated yield (white powder): 1.59 g (94.4 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 12.00 (s, 2H), 7.68 (d, *J* = 8.4 Hz, 4H), 6.60 (d, *J* = 8.5 Hz, 4H), 6.51 (t, *J* = 5.2 Hz, 2H), 3.32 – 3.21 (m, 4H). ^{13}C NMR (50.32 MHz, DMSO-d_6, 298 K): δ =167.4, 152.4, 131.2, 117.1, 110.9, 41.4. IR (diamond ATR): $\tilde{\nu}$ = 425 (w), 501 (s), 558 (s), 630 (m), 642 (m), 697 (s), 768 (vs), 785 (w), 815 (m), 845 (m), 855 (m), 931 (s), 962 (m), 1092 (m), 1118 (s), 1179 (vs), 1252 (vs), 1294 (vs), 1317 (vs), 1338 (vs), 1427 (vs), 1477 (s), 1493 (s), 1528 (s), 1578 (vs), 1599 (vs), 1665 (vs), 1931 (w), 2543 (m), 2664 (m), 2856 (m), 2901 (m), 2953 (m), 3411 (m). T_d (TGA) = 252 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{17}N_2O_4^+$, 301.1183; found, 301.1168.

Experimental data for 13. Formamide 1b (2 g, 5.4 mmol), sodium hydroxide (2.16 g, 54 mmol); isolated yield (yellow powder): 1.58 g (93.1 %). ^{1}H NMR (200.13 MHz, DMSO-d_6, 298 K): δ = 11.96 (s, 2H), 7.67 (d, *J* = 8.3 Hz, 4H), 6.58 (d, *J* = 8.4 Hz, 4H), 6.47 (t, *J* = 5.4 Hz, 2H), 3.17 (q, *J* = 6.5 Hz, 4H), 1.83 (p, *J* = 6.9 Hz, 2H). ^{13}C NMR (50.32 MHz, DMSO-d_6, 298 K): δ = 167.5, 152.6, 131.1, 116.8, 110.8, 40.1, 27.8. IR (diamond ATR): $\tilde{\nu}$ = 407 (w), 419 (w), 499 (m), 555 (m), 635 (m), 655 (m), 696 (s), 765 (vs), 805 (m), 834 (vs), 941 (m), 1058 (m), 1081 (m), 1103 (m), 1128 (s), 1141 (m), 1174 (vs), 1245 (s), 1292 (vs), 1314

(vs), 1346 (s), 1425 (s), 1471 (m), 1489 (m), 1528 (s), 1576 (s), 1601 (vs), 1662 (vs), 1922 (w), 2540 (m), 2659 (m), 2863 (m), 2935 (m), 3420 (m). T_d (TGA) = 232.1 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{19}N_2O_4^+$, 315.1339; found, 315.1320.

Experimental data for 14. Formamide 1c (2 g, 5.2 mmol), sodium hydroxide (2.08 g, 52 mmol); isolated yield (white powder): 1.60 g (93.7 %). ^{1}H NMR (200.13 MHz, DMSO-d_6, 298 K): δ = 11.94 (s, 2H), 7.66 (d, *J* = 8.4 Hz, 4H), 6.56 (d, *J* = 8.6 Hz, 4H), 6.42 (t, *J* = 5.4 Hz, 2H), 3.23 – 2.93 (m, 4H), 1.85 – 1.42 (m, 4H). ^{13}C NMR (50.32 MHz, DMSO-d_6, 298 K): δ = 167.5, 152.7, 131.1, 116.6, 110.7, 42.1, 26.1. IR (diamond ATR): $\tilde{\nu}$ = 427 (w), 476 (m), 503 (s), 518 (m), 556 (s), 635 (s), 653 (s), 699 (s), 742 (s), 771 (vs), 791 (m), 833 (vs), 844 (s), 856 (m), 936 (s), 968 (m), 1030 (m), 1090 (m), 1121 (vs), 1177 (vs), 1236 (m), 1286 (vs), 1297 (vs), 1319 (vs), 1341 (vs), 1428 (vs), 1445 (m), 1477 (s), 1528 (s), 1574 (s), 1604 (vs), 1662 (vs), 1933 (w), 2546 (m), 2661 (m), 2845 (m), 2860 (m), 2887 (m), 2932 (m), 3423 (m). T_d (TGA) = 273.9 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{18}H_{21}N_2O_4^+$, 329.1496; found, 329.1479.

Experimental data for 15. Formamide 3a (2 g, 5.6 mmol), sodium hydroxide (2.25 g, 56 mmol); isolated yield (white powder): 1.65 g (97.9 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 12.64 (s, 2H), 7.22 – 7.16 (m, 4H), 7.13 (dt, *J* = 7.6, 1.3 Hz, 2H), 6.82 (ddd, *J* = 8.1, 2.5, 1.2 Hz, 2H), 5.95 (m, 2H), 3.26 (m, 4H). ^{13}C NMR (50.32 MHz, DMSO-d_6, 298 K): δ = 167.8, 148.7, 131.4, 129, 116.7, 116.2, 112.5, 41.9. IR (diamond ATR): $\tilde{\nu}$ = 418 (w), 467 (w), 524 (m), 546 (m), 562 (m), 598 (w), 634 (m), 668 (s), 676 (s), 745 (vs), 776 (m), 806 (m), 818 (m), 857 (m), 867 (s), 933 (s), 993 (m), 1070 (m), 1091 (m), 1124 (m), 1171 (m), 1263 (vs), 1301 (vs), 1325 (s), 1417 (s), 1435 (s), 1471 (s), 1508 (s), 1585 (vs), 1601 (vs), 1675 (vs), 2549 (m), 2843 (m), 3397 (m). T_d (TGA) = 222 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{17}N_2O_4^+$, 301.1183; found, 301.1170.

Experimental data for 16. Formamide 3b (2 g, 5.4 mmol), sodium hydroxide (2.16 g, 54 mmol); isolated yield (yellow powder): 1.6 g (94.3 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 12.62 (s, 2H), 7.22 – 7.13 (m, 4H), 7.11 (dt, *J* = 7.6, 1.3 Hz, 2H), 6.79 (ddd, *J* = 7.9, 2.4, 1.2 Hz, 2H), 5.91 (m, 2H), 3.14 (t, *J* = 6.9 Hz, 4H), 1.84 (p, *J* = 6.9 Hz, 2H). ^{13}C NMR (50.32 MHz, DMSO-d_6, 298 K): δ = 167.9, 149, 131.4, 128.9, 116.5, 116.1, 112.5, 40.7, 27.9. IR (diamond ATR): $\tilde{\nu}$ = 427 (m), 468 (w), 537 (m), 552 (m), 567 (m), 675 (s), 749 (vs), 783 (m), 803 (m), 862 (m), 889 (m), 914 (m), 992 (m), 1048 (m), 1093 (s), 1115 (s), 1140 (m), 1234 (s), 1257 (vs), 1272 (vs), 1292 (s), 1309 (s), 1411 (m), 1442 (s), 1472 (s), 1506 (m), 1583 (vs), 1602 (vs), 1675 (vs), 1932 (w), 2527 (m), 2641 (m), 2839 (m), 2950 (m), 3405 (w), 3429 (w). T_d (TGA) = 218.1 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{19}N_2O_4^+$, 315.1339; found, 315.1322.

Experimental data for 17. Formamide 3c (2 g, 5.2 mmol), sodium hydroxide (2.08 g, 52 mmol); isolated yield (white powder): 1.56 g (91.3 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 12.64 (s, 2H), 7.24 – 7.01 (m, 6H), 6.78 (d, *J* = 8.0 Hz, 2H), 5.87 (m, 2H), 3.05 (m, 4H), 1.65 (m, 4H). ^{13}C NMR (50.32 MHz, DMSO-d_6, 298 K): δ = 167.9, 149.1, 131.4, 128.9, 116.3, 115.9, 112.4, 42.6, 26.3. IR (diamond ATR): $\tilde{\nu}$ = 423 (w), 449 (w), 536 (w), 556 (m), 668 (s), 748 (vs), 779 (w), 799 (w), 858 (m), 887 (w), 941 (s), 994 (m), 1075 (m), 1098 (m), 1125 (m), 1168 (w), 1234 (m), 1267 (vs), 1286 (vs), 1349 (m), 1378 (w), 1410 (m), 1441 (s), 1472 (m), 1512 (m), 1588 (s), 1601 (s), 1668 (vs), 1924 (vw), 2517 (w), 2642 (w), 2868 (m), 2938 (m), 2938 (m). T_d (TGA) = 215.2 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{18}H_{21}N_2O_4^+$, 329.1496; found, 329.1479.

Experimental data for 18. Formamide 5a (2 g, 5.6 mmol), sodium hydroxide (2.25 g, 56 mmol); isolated yield (white powder): 1.556 g (92.3 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 12.27 (s, 2H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.34 – 6.99 (m, 2H), 6.81 (d, *J* = 7.9 Hz, 1H), 6.72 – 6.32 (m, 4H), 5.99 (m, 1H), 3.32 – 3.15 (m, 4H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K): δ = 168, 167.6, 152.4, 148.7, 131.7, 131.3, 129.1, 117.1, 116.8, 116.2,

112.5, 110.9, 41.8, 41.4. IR (diamond ATR): $\tilde{\nu}$ = 427 (w), 502 (w), 553 (w), 629 (w), 667 (w), 698 (w), 749 (m), 771 (m), 814 (w), 838 (m), 874 (w), 934 (w), 1124 (m), 1176 (m), 1291 (s), 1313 (m), 1428 (m), 1462 (w), 1494 (w), 1527 (m), 1603 (m), 1668 (m), 2854 (w) cm^{-1}. T_d (TGA) = 198.6 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{17}N_2O_4^+$, 301.1183; found, 301.1171.

Experimental data for 19. Formamide 5b (2 g, 5.4 mmol), sodium hydroxide (2.16 g, 54 mmol); isolated yield (yellow powder): 1.613 g (95 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 12.27 (s, 2H), 7.66 (d, *J* = 8.2 Hz, 2H), 7.27 – 7.05 (m, 2H), 6.79 (d, *J* = 8.0 Hz, 1H), 6.72 – 6.32 (m, 4H), 5.94 (m, 1H), 3.15 (dq, *J* = 22.4, 7.5, 6.8 Hz, 4H), 1.83 (p, *J* = 7.0 Hz, 2H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K): δ = 168, 167.6, 152.7, 149, 131.4, 131.2, 129, 116.7, 116.7, 116.5, 116.2, 112.5, 110.8, 40.6, 27.9. IR (diamond ATR): $\tilde{\nu}$ = 418 (w), 503 (m), 553 (w), 646 (w), 681 (w), 698 (w), 752 (s), 770 (m), 836 (m), 868 (w), 936 (m), 1115 (m), 1175 (vs), 1286 (s), 1316 (s), 1426 (m), 1466 (m), 1488 (m), 1528 (m), 1600 (vs), 1668 (s), 2542 (w), 2865 (w), 3413 (w) cm^{-1}. T_d (TGA) = 198.5 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{19}N_2O_4^+$, 315.1339; found, 315.1325.

Experimental data for 20. Formamide 5c (2 g, 5.2 mmol), sodium hydroxide (2.08 g, 52 mmol); isolated yield (white powder): 1.572 g (92 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 12.27 (s, 2H), 7.65 (d, *J* = 8.3 Hz, 2H), 7.19 – 7.05 (m, 2H), 6.77 (d, *J* = 8.0 Hz, 1H), 6.71 – 6.26 (m, 3H), 5.90 (m, 1H), 3.16 – 2.96 (m, 4H), 1.81 – 1.49 (m, 4H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K): δ = 168.1, 167.6, 152.7, 149.1, 131.7, 131.2, 128.9, 116.6, 116.4, 115.9, 112.5, 110.7, 42.6, 42.2, 42.1, 26.2. IR (diamond ATR): $\tilde{\nu}$ = 427 (vw), 503 (w), 553 (w), 648 (w), 680 (w), 699 (w), 746 (m), 772 (m), 836 (m), 863 (w), 938 (w), 994 (w), 1124 (m), 1177 (m), 1292 (m), 1315 (m), 1344 (m), 1429 (m), 1470 (m), 1531 (w), 1605 (vs), 1668 (s), 2862 (w), 2933 (w), 3418 (w) cm^{-1}. T_d (TGA) = 204.9 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{18}H_{21}N_2O_4^+$, 329.1496; found, 329.1480.

Experimental data for 21. Formamide 7a (2 g, 6.06 mmol), sodium hydroxide (2.42 g, 60.6 mmol); isolated yield (yellow powder): 1.69 g (92.3 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 8.00 (d, *J* = 9.2 Hz, 4H), 7.39 (d, *J* = 5.1 Hz, 2H), 6.68 (d, *J* = 9.3 Hz, 4H), 3.49 – 3.35 (m, 4H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K): δ = 154.4, 135.9, 126.2, 110.9, 41.3. IR (diamond ATR): $\tilde{\nu}$ = 423 (w), 446 (w), 480 (m), 538 (m), 619 (w), 649 (w), 698 (m), 749 (m), 824 (s), 852 (w), 887 (m), 995 (m), 1064 (m), 1091 (m), 1178 (m), 1226 (m), 1281 (s), 1466 (m), 1503 (w), 1538 (m), 1592 (s), 2929 (w), 3370 (m). T_d (TGA) = 262.9 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{14}H_{15}N_4O_4^+$, 303.1088; found, 303.1088.

Experimental data for 22. Formamide 7b (2 g, 5.8 mmol), sodium hydroxide (2.32 g, 58 mmol); isolated yield (yellow powder): 1.77 g (96.3 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 7.99 (d, *J* = 8.8 Hz, 4H), 7.33 (t, *J* = 5.4 Hz, 2H), 6.65 (d, *J* = 9.0 Hz, 4H), 3.26 (q, *J* = 6.5 Hz, 4H), 1.87 (p, *J* = 7.0 Hz, 2H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K): δ = 154.5, 135.6, 126.2, 110.8, 40, 27.5. IR (diamond ATR): $\tilde{\nu}$ = 420 (m), 457 (m), 486 (vs), 536 (vs), 620 (m), 641 (m), 659 (m), 693 (s), 748 (vs), 804 (m), 824 (vs), 898 (m), 940 (s), 995 (vs), 1085 (vs), 1103 (vs), 1179 (s), 1206 (vs), 1268 (vs), 1286 (vs), 1305 (vs), 1318 (vs), 1338 (vs), 1434 (m), 1457 (s), 1477 (s), 1539 (vs), 1594 (vs), 2855 (w), 3341 (s). T_d (TGA) = 275.3 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{15}H_{17}N_4O_4^+$, 317.1244; found, 317.1246.

Experimental data for 23. Formamide 7c (2 g, 5.58 mmol), sodium hydroxide (2.23 g, 55.8 mmol); isolated yield (yellow powder): 1.75 g (94.9 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 7.98 (d, *J* = 8.9 Hz, 4H), 7.31 (t, *J* = 5.5 Hz, 2H), 6.64 (d, *J* = 9.0 Hz, 4H), 3.28 – 3.11 (m, 4H), 1.78 – 1.56 (m, 4H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K): δ = 154.5, 135.4, 126.2, 110.6, 42, 25.8. IR (diamond ATR): $\tilde{\nu}$ = 428 (m), 487 (m), 522 (w), 546 (w), 603 (m), 641 (w), 693 (m), 751 (m), 799 (w), 826 (m), 961 (m), 996 (m), 1103 (s), 1124 (m), 1173 (m), 1227 (m), 1273 (s), 1297 (s), 1350 (w), 1382 (w), 1464 (m), 1540 (m), 1599 (m),

2955 (w), 3355 (w). T_d (TGA) = 257.5 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{19}N_4O_4^+$, 331.1401; found, 331.1402.

Experimental data for 24. Formamide 8a (2 g, 5.02 mmol), sodium hydroxide (2.01 g, 50.2 mmol); isolated yield (off-white powder): 1.79 g (96.3 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 7.2 (d, *J* = 8.8 Hz, 4H), 6.54 (d, *J* = 8.8 Hz, 4H), 5.87 (t, *J* = 5.1 Hz, 2H), 3.26 – 3.09 (m, 4H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K): δ = 147.9, 131.4, 113.9, 106.2, 41.9. IR (diamond ATR): $\tilde{\nu}$ = 505 (m), 693 (w), 806 (s), 946 (w), 992 (w), 1067 (m), 1121 (m), 1177 (m), 1242 (m), 1317 (m), 1398 (w), 1477 (m), 1503 (m), 1588 (m), 2849 (w), 3406 (w). T_d (TGA) = 204.3 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{14}H_{15}Br_2N_2^+$, 370.9576; found, 370.9577.

Experimental data for 25. Formamide 8b (2 g, 4.85 mmol), sodium hydroxide (1.94 g, 48.5 mmol); isolated yield (off-white powder): 1.81 g (97.1 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 7.18 (d, *J* = 8.8 Hz, 4H), 6.51 (d, *J* = 8.9 Hz, 4H), 5.84 (t, *J* = 5.5 Hz, 2H), 3.06 (q, *J* = 6.5 Hz, 4H), 1.78 (p, *J* = 6.9 Hz, 2H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K): δ = 148.1, 131.3, 113.8, 105.9, 40.5, 27.8. IR (diamond ATR): $\tilde{\nu}$ = 505 (s), 654 (m), 696 (m), 767 (m), 811 (vs), 994 (m), 1070 (s), 1122 (m), 1138 (m), 1178 (s), 1202 (m), 1250 (s), 1295 (s), 1315 (s), 1398 (m), 1472 (vs), 1493 (vs), 1590 (vs), 1673 (w), 1874 (w), 2837 (m), 2926 (m), 3397 (m). T_d (TGA) = 195.3 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{15}H_{17}Br_2N_2^+$, 384.9733; found, 384.9733.

Experimental data for 26. Formamide 8c (2 g, 4.69 mmol), sodium hydroxide (1.88 g, 46.9 mmol); isolated yield (off-white powder): 1.82 g (97.4 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 7.17 (d, *J* = 8.4 Hz, 4H), 6.50 (d, *J* = 8.4 Hz, 4H), 5.80 (t, *J* = 5.6 Hz, 2H), 3.07 – 2.91 (m, 4H), 1.70 – 1.52 (m, 4H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K): δ = 148.2, 131.3, 113.7, 105.8, 42.5, 26.2. IR (diamond ATR): $\tilde{\nu}$ = 418 (w), 504 (s), 648 (m), 693 (w), 749 (m), 810 (vs), 997 (m), 1067 (m), 1085 (m), 1120 (m), 1177 (s), 1191 (m), 1227 (m), 1264 (m), 1294 (m), 1308 (m), 1323 (m), 1395 (m), 1448 (m), 1471 (s), 1494 (s), 1590 (s), 2824 (m), 2941 (m), 3397 (m). T_d (TGA) = 197.3 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{19}Br_2N_2^+$, 398.9889; found, 398.9889.

Experimental data for 27. Formamide 9a (2 g, 6.66 mmol), sodium hydroxide (2.66 g, 66.6 mmol); isolated yield (brown powder): 1.53 g (84.4 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 6.71 (d, *J* = 8.9 Hz, 4H), 6.54 (d, *J* = 8.9 Hz, 4H), 5.17 (t, *J* = 5.5 Hz, 2H), 3.63 (s, 6H), 3.22 – 3.05 (m, 4H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K): δ = 150.7, 143, 114.6, 113.1, 55.3, 43.1. IR (diamond ATR): $\tilde{\nu}$ = 408 (w), 467 (m), 511 (m), 611 (m), 643 (m), 754 (w), 814 (vs), 836 (m), 942 (w), 1030 (vs), 1077 (m), 1118 (m), 1178 (s), 1228 (vs), 1266 (s), 1285 (m), 1407 (m), 1440 (m), 1463 (s), 1506 (vs), 1668 (w), 2835 (w), 2898 (w), 2952 (w), 3358 (w). T_d (TGA) = 209.9 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{21}N_2O_2^+$, 273.1598; found, 273.1598.

Experimental data for 28. Formamide 9b (2 g, 6.36 mmol), sodium hydroxide (2.54 g, 63.6 mmol); isolated yield (brown powder): 1.49 g (81.8 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 6.70 (d, *J* = 8.9 Hz, 4H), 6.52 (d, *J* = 8.9 Hz, 4H), 5.13 (br s, 2H), 3.63 (s, 6H), 3.03 (t, *J* = 6.9 Hz, 4H), 1.77 (p, *J* = 7.0 Hz, 2H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K): δ = 150.5, 143.3, 114.6, 113, 55.3, 41.7, 28.5. IR (diamond ATR): $\tilde{\nu}$ = 520 (w), 600 (w), 716 (w), 762 (w), 777 (w), 818 (m), 1029 (m), 1088 (w), 1138 (w), 1177 (m), 1232 (m), 1253 (m), 1303 (w), 1335 (w), 1407 (w), 1440 (w), 1455 (m), 1511 (m), 1618 (w), 2832 (w), 2931 (w), 3377 (w). T_d (TGA) = 201.5 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{23}N_2O_2^+$, 287.1754; found, 287.1750.

Experimental data for 29. Formamide 9c (2 g, 6.09 mmol), sodium hydroxide (2.44 g, 60.9 mmol); isolated yield (brown powder): 1.53 g (83.6 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 6.69 (d, *J* = 8.9 Hz, 4H), 6.51 (d, *J* = 8.9 Hz, 4H), 5.09 (br s, 2H), 3.62 (s, 6H), 3.05 – 2.86 (m, 4H), 1.73 – 1.50 (m, 4H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K): δ =

150.4, 143.4, 114.6, 112.9, 55.3, 43.6, 26.6. IR (diamond ATR): $\tilde{\nu}$ = 459 (m), 529 (vw), 577 (vw), 768 (w), 819 (m), 956 (w), 998 (w), 1028 (s), 1082 (s), 1175 (m), 1235 (m), 1300 (w), 1405 (vw), 1449 (w), 1473 (w), 1514 (m), 1618 (vw), 2835 (vw), 3378 (w). T_d (TGA) = 195.3 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{18}H_{25}N_2O_2^+$, 301.1911; found, 301.1912.

Experimental data for 30. Formamide 10a (2 g, 5.02 mmol), sodium hydroxide (2.01 g, 50.2 mmol); isolated yield (brown oil): 1.7 g (91.4 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 7.01 (t, *J* = 8.0 Hz, 2H), 6.73 (t, *J* = 2.1 Hz, 2H), 6.66 (dd, *J* = 7.8, 1.8 Hz, 2H), 6.57 (dd, *J* = 8.2, 2.2 Hz, 2H), 6.21 – 5.71 (m, 2H), 3.26 – 3.12 (m, 4H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K): δ = 150.3, 130.7, 122.4, 117.9, 114, 111, 41.6. IR (diamond ATR): $\tilde{\nu}$ = 434 (s), 522 (w), 679 (vs), 758 (vs), 835 (vs), 932 (m), 984 (vs), 1067 (vs), 1084 (s), 1117 (m), 1166 (s), 1247 (vs), 1279 (s), 1320 (vs), 1364 (m), 1417 (s), 1465 (vs), 1479 (vs), 1496 (vs), 1571 (vs), 1590 (vs), 1916 (w), 2854 (m), 3401 (m). T_d (TGA) = 243.5 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{14}H_{15}Br_2N_2^+$, 370.9576; found, 370.9575.

Experimental data for 31. Formamide 10b (2 g, 4.85 mmol), sodium hydroxide (1.94 g, 48.5 mmol); isolated yield (yellow oil): 1.75 g (93.9 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 6.99 (t, *J* = 8.0 Hz, 2H), 6.71 (t, *J* = 2.1 Hz, 2H), 6.63 (dd, *J* = 7.7, 1.8 Hz, 2H), 6.55 (dd, *J* = 8.3, 2.2 Hz, 2H), 5.95 (t, *J* = 5.5 Hz, 2H), 3.08 (q, *J* = 6.5 Hz, 4H), 1.78 (p, *J* = 6.9 Hz, 2H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K): δ = 150.6, 130.7, 122.4, 117.6, 113.9, 110.9, 40.3, 27.8. IR (diamond ATR): $\tilde{\nu}$ = 435 (s), 492 (w), 572 (w), 680 (vs), 757 (vs), 835 (vs), 984 (vs), 1066 (vs), 1084 (s), 1132 (m), 1165 (s), 1200 (m), 1244 (s), 1280 (s), 1322 (vs), 1416 (s), 1470 (vs), 1480 (vs), 1497 (vs), 1571 (vs), 1591 (vs), 2856 (m), 2932 (m), 3408 (m). T_d (TGA) = 262.2 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{15}H_{17}Br_2N_2^+$, 384.9733; found, 384.9732.

Experimental data for 32. Formamide 10c (2 g, 4.69 mmol), sodium hydroxide (1.88 g, 46.9 mmol); isolated yield (rose-colored crystals): 1.74 g (93.1 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 6.98 (t, *J* = 8.0 Hz, 2H), 6.70 (t, *J* = 2.1 Hz, 2H), 6.62 (dd, *J* = 7.7, 1.8 Hz, 2H), 6.54 (dd, *J* = 8.2, 2.2 Hz, 2H), 5.91 (t, *J* = 5.4 Hz, 2H), 3.01 (q, *J* = 5.9 Hz, 4H), 1.69 – 1.53 (m, 4H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K): δ = 150.6, 130.6, 122.4, 117.5, 113.8, 110.8, 42.3, 26.1. IR (diamond ATR): $\tilde{\nu}$ = 439 (m), 660 (m), 682 (vs), 760 (vs), 830 (s), 871 (w), 904 (w), 982 (s), 1062 (m), 1078 (m), 1103 (m), 1134 (m), 1163 (m), 1270 (s), 1282 (s), 1321 (s), 1359 (m), 1416 (s), 1453 (s), 1467 (s), 1500 (vs), 1563 (s), 1594 (vs), 2860 (m), 2924 (m), 3394 (m), 3417 (s). T_d (TGA) = 262.3 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{19}Br_2N_2^+$, 398.9889; found, 398.9889.

Experimental data for 33. Formamide 11a (2 g, 7.45 mmol), sodium hydroxide (2.98 g, 74.5 mmol); isolated yield (yellow oil): 1.54 g (86 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 6.95 (t, *J* = 7.6 Hz, 2H), 6.43 – 6.31 (m, 6H), 5.50 (d, *J* = 5.6 Hz, 2H), 3.24 – 3.10 (m, 4H), 2.18 (s, 6H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K): δ = 148.7, 137.9, 128.8, 116.6, 112.6, 109.4, 42.1, 21.4. IR (diamond ATR): $\tilde{\nu}$ = 441 (vs), 452 (m), 542 (s), 585 (vs), 690 (vs), 766 (vs), 812 (m), 855 (m), 871 (vs), 909 (m), 961 (m), 994 (m), 1090 (vs), 1170 (vs), 1178 (vs), 1202 (m), 1264 (vs), 1289 (s), 1325 (vs), 1375 (m), 1456 (s), 1487 (vs), 1524 (vs), 1590 (vs), 2874 (m), 2914 (s), 3033 (m), 3300 (m). T_d (TGA) = 207.4 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{21}N_2^+$, 241.1699; found, 241.1697.

Experimental data for 34. Formamide 11b (2 g, 7.08 mmol), sodium hydroxide (2.83 g, 70.8 mmol); isolated yield (brown oil): 1.6 g (88.9 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 6.93 (t, *J* = 7.7 Hz, 2H), 6.44 – 6.26 (m, 6H), 5.47 (t, *J* = 5.7 Hz, 2H), 3.07 (q, *J* = 6.5 Hz, 4H), 2.16 (s, 6H), 1.79 (p, *J* = 6.9 Hz, 2H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K): δ = 149, 137.7, 128.7, 116.3, 112.5, 109.4, 40.7, 28.3, 21.4. IR (diamond ATR): $\tilde{\nu}$ = 440 (s), 525 (vw), 579 (w), 691 (vs), 765 (vs), 843 (m), 919 (vw), 992 (m), 1035 (w), 1128 (m), 1167 (s), 1179 (s), 1263 (s), 1302 (s), 1327 (s), 1376 (w), 1489 (vs), 1508 (vs), 1587 (vs),

1603 (vs), 2858 (m), 2918 (m), 3039 (w), 3402 (w). T_d (TGA) = 207.9 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{23}N_2^+$, 255.1856; found, 255.1851.

Experimental data for 35. Formamide 11c (2 g, 6.75 mmol), sodium hydroxide (2.7 g, 67.5 mmol); isolated yield (brown oil): 1.59 g (87.8 %). ^{1}H NMR (400.13 MHz, DMSO-d_6, 298 K): δ = 6.93 (t, *J* = 7.6 Hz, 2H), 6.42 – 6.28 (m, 6H), 5.41 (t, *J* = 5.6 Hz, 2H), 3.00 (q, *J* = 5.9 Hz, 4H), 2.17 (s, 6H), 1.71 – 1.54 (m, 4H). ^{13}C NMR (100.61 MHz, DMSO-d_6, 298 K): δ = 149, 137.7, 128.7, 116.3, 112.5, 109.2, 42.7, 26.5, 21.4. IR (diamond ATR): $\tilde{\nu}$ = 440 (m), 527 (vw), 580 (vw), 691 (vs), 767 (vs), 843 (w), 992 (m), 1092 (m), 1167 (m), 1179 (m), 1259 (m), 1303 (m), 1328 (s), 1375 (w), 1490 (s), 1509 (s), 1588 (vs), 1603 (vs), 2858 (m), 2919 (m), 3040 (w), 3402 (w). T_d (TGA) = 199.4 °C. HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{18}H_{25}N_2^+$, 269.2012; found, 269.2010.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: XXX.

Summary of attempts for one-step synthesis

MALDI-TOF MS spectra

Crystallographic data and X-ray structures

^{1}H, ^{13}C, HSQC (^{1}H-^{13}C) and COSY (^{1}H-^{1}H) NMR spectra of the compounds described in the Experimental Section

TGA curves

HRMS spectra of the compounds described in the Experimental Section

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Notes

The authors declare no competing financial interest.

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