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Catalyst free C–N bond formation by the reaction of amines with diimides: Bulky guanidines†

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We have shown an atom economical and catalyst free addition of cyclic secondary amines to various bulky aryl symmetrical and unsymmetrical carbodiimides to afford *N,N'N"N"*-tetra substituted guanidines in quantitative yields at ambient reaction conditions. Further, addition of diamine to bulky aryl symmetrical carbodiimides (2 equiv.) to the formation of bulky aryl biguanidines was established.

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†Electronic supplementary information (ESI) available: ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra for compounds **1a** – **28a** and X-ray crystal data and bond parameters for compounds **1a**, **22a** and **27a.**

Introduction

Guanidines are organic compounds consisting of triangular array of nitrogen atoms surrounding a carbon atom. The general formula of guanidines is R_1-N=C(NR_2R_3)NR_4R_5, in which carbon atom of N_3C functional group, which is connected to one imino and two amino nitrogen atoms. Guanidines are stronger bases[1,2] than other nitrogen compounds such as pyridines, amines, diamines and amidines. And also, biguanidines are even more basic than the classical "proton sponge". Thus, guanidines have been employed in various base catalyzed reactions.[3] Chiral organocatalysts containing N_3C moiety, *i.e.* chiral guanidines[4] have been utilized as asymmetric catalysts for different reactions.[5,6] The guanidine moiety is an essential substructure in many biologically and pharmaceutically important molecules and also natural products.[7] More importantly, negatively charged guanidinates play a vital role in stabilizing several complexes of various elements of the periodic table.[8] In 2006, Coles in his excellent review pointed out that guanidine framework constitutes a versatile ligand set for use in coordination chemistry.[9] Thus, guanidines are useful N-donor ligands in coordination chemistry. Further, guanidinate supported metal complexes have been utilized in catalysis[10] and polymerization reactions.[11]

Generally, synthesis of guanidines can be achieved by two routes. The first synthetic route *i.e.*, 'classical guanidine synthesis' uses reagents named as 'guanylating agents' by Katrizky and coworkers,[12] which is mainly based on stoichiometric reactions. By using this route, guanidine unit can be built up by chemical transformation from amidine, sulfonic acids, carbodiimides, cynamides and isothiourea etc.; however, all those methods mentioned above suffer from poor yields, multiple steps, costly reagents and some cases toxic chemicals, non availability of suitable precursors and harsh reaction conditions.

Secondly, synthesis of guanidines can be achieved by the utilization of organometallic and coordination compounds, which is based on catalytic processes. In this regard few review articles appeared in the literature.[13,14] More importantly, Zhang and coworkers have shown four types of mechanisms for catalytic guanylation of amines with carbodiimides.[15] Recently, Carrillo-Hermosilla et al., described nicely on catalytic synthesis of guanidines.[16]

Although, two research groups namely Jones and Gagliardi&Kempe have reported the addition of metallated amides to *N,N'*-diaryl substituted carbodiimides, followed by aqueous work-up afford the tetra-substituted guanidines, but this synthetic route is limited to a very few bulky aryl guanidines.[17,18] Disadvantages for this method are the limited availability of *N,N'*-diaryl substituted carbodiimides and addition of metallated amide to carbodiimide in air and moisture free conditions. Thus, it is very clear that *N,N'*-diarylcarbodiimides are important precursors for the preparation of bulky guanidine type ligands, even related bulky amidines. Generally, bulky aryl carbodimides can be synthesized by corresponding thioureas on treatment with toxic mercuric oxide and anhydrous magnesium sulphate in toluene at boiling temperature.[19] Recently, our group found an easy access of various symmetrical and unsymmetrical *N,N'*-diaryl substituted carbodiimides by the desulphurization of corresponding thiourea using thiophilic agent and base.[20]

It is documented that carbodiimides react with primary aliphatic amines, in the absence of a catalyst, to generate the corresponding guanidines at harsh reaction conditions.[21] However, direct addition of aromatic amines or cyclic secondary amines with carbodimides cannot be achieved without catalysts due to their decreased nucleophilicity. Moreover, addition of aromatic or cyclic secondary amines is restricted to commercially available aliphatic carbodiimides such as dicyclohexylcarbodiimide (DCC), diisopropylcarbodiimide (DICDI) etc., in the presence of a wide range of metal catalysts.[22] Very recently, we have reported N-heterocyclic carbene (NHC) supported magnesium bis(amide) complex as an

efficient catalyst for the guanylation reaction.[23] To the best of our knowledge no reports on the catalyst free addition of cyclic secondary amines to *N,N'*-diaryl substituted carbodiimides.

Guanidines can be broadly classified as mono, *N,N'*-di, *N,N',N"*-tri and *N,N',N",N"*-tetra-substituted. Above all tetra-substituted guanidinate anions are important precursors to isolate unusual metal complexes, particularly low valent and/or low oxidation state.[24] For instance, Jones research group reported guanidinate stabilized magnesium(I) dimer with Mg–Mg bond, where magnesium oxidation state is +1.[25] This was achieved due to the steric and bulky nature of guanidinate anion. Very recently, we have reported bulky guanidinate supported low valent Ge(II) and Sn(II) amide complexes.[26] Thus, bulky guanidine ligand systems are important precursors in isolating unusual metal complexes.

Considering the importance of such bulky aryl guanidine systems in isolating unusual metal complexes, our attention turned to find an easy access of *N,N',N",N"*- tetra-substituted guanidines. Herein we report a catalyst free C–N bond formation in guanylation reaction by the addition of cyclic secondary amines to various bulky aryl symmetrical and unsymmetrical carbodiimides to afford *N, N',N",N"*- tetra-substituted guanidines.

Results and discussion

A sp hybridized carbon atom of N=C=N core of carbodiimides, which is more elctrophilic in *N,N'*-diaryl substituted carbodiimides compare to aliphatic carbodiimides. Taking an advantage of high electrophilic nature of carbon atom of N=C=N moiety in *N,N'*-diaryl substituted carbodiimides; we have treated cyclic secondary amines to various bulky aryl symmetrical and unsymmetrical carbodimides to obtain tetra-substituted acyclic guanidines.

Our investigations began with the reaction of *N,N'*-diaryl substituted carbodiimide with cyclic secondary amine at room temperature either in hydrocarbon or ethereal solvent. We were pleased to notice that cyclic secondary amines react with *N,N'*-diaryl substituted carbodiimide to give tetra-substituted guani-

dine's at ambient temperature condition (**1a – 24a**) in very good to excellent yields, except for compounds **19a** and **20a**. The poor yield obtained for compounds **19a(**42%**)** and **20a(**37%) respectively, even at elevated temperature; probably because of steric congestion. Saying that in both cases, ortho methyl substituent's attached in secondary amine (2,6-Dimethylpiperidine) hinders the addition of amine N-H bond to the C=N double bond of the carbodiimide. After these results, we were interested to explore the catalyst free addition of unsymmetrical *N,N*- diary substituted carbodiimide with cyclic secondary amines. To our delight those reactions resulted in excellent yields (**25a & 26a**). Further, addition of two equivalents of symmetric *N,N*-diaryl substituted carbodiimides to the piperazine in thf led to the formation of biguanidines (**27a & 28a**) in moderate to good yields at room or reflux temperature. All products were characterized by ^{1}H, ^{13}C NMR, IR and mass spectrometry analyses. Furthermore, products **1a**, **22a** and **27a** have been confirmed by single crystal X-ray structural analysis.

For compounds **1a-24a,** display simple ^{1}H and ^{13}C NMR spectra, this indicates the presence of only one isomer in solution. In ^{1}H NMR spectra the singlet NH resonance has been observed in the range of 4.94 – 5.52 ppm for the symmetrical tetra-substituted guanidines(**1a – 24a).** In case of unsymmetrical tetra-substituted guanidines (**25a & 26a**), the NH peak is showing two broad singlets in the range of 4.96 – 5.10 ppm indicating the presence of two isomeric forms of guanidine in solution. In biguanidines (**27a & 28a**) both NH protons show a singlet peak at 5.03, indicates the symmetrical behavior of the molecules and also only one isomeric form *i.e*., Z_{anti} at both the guanidine moieties. In ^{13}C NMR spectra, all compounds (**1a – 28a**) show a significant peak for the N_3C carbon atom in the range of 148.2 – 152.2 ppm, which is well in agreement with the reported guanidines (148-160 ppm).[9,20] And also, all compounds were confirmed by IR spectra, where it is showing the functional groups for NH and C=N peaks in the range of 3317 – 3394 cm^{-1} and 1610 – 1631 cm^{-1} respectively. Furthermore, purity of newly synthesized compound was confirmed by HRMS analysis.

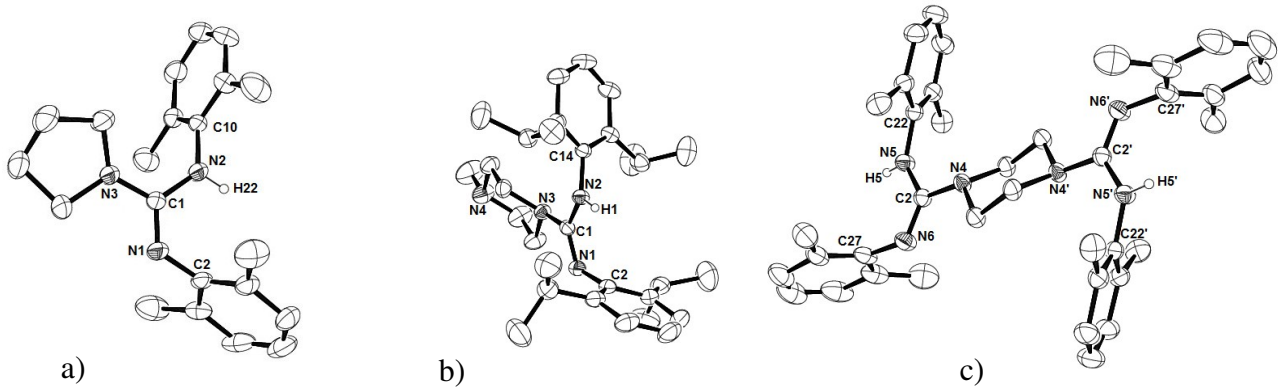
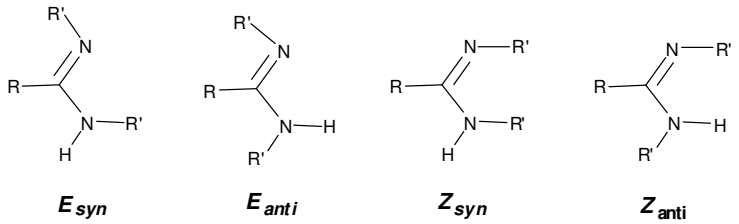


Fig.1. Molecular structures for a) **1a**, b) **22a** and c) **27a**, probability density 30%; H-atoms (except N–H bond) are omitted for clarity.

The molecular structures for **1a**, **22a** and **27a** are presented in Figure 1 and selected bond lengths and bond angles are provided in the supporting information (Table S3). Concerning the tetra-substituted guanuidines, the rotation and isomerization around the C–N & C=N bond, forms four different tautomeric structures as E_{syn}, E_{anti}, Z_{syn} & Z_{anti} (see Scheme 1).[9]



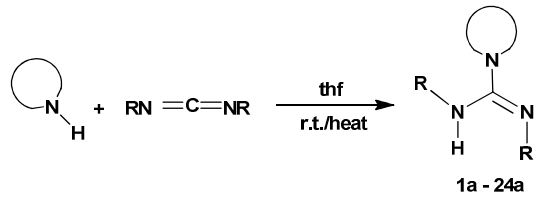
Scheme 1. Four different conformations of tetra-substituted guanidine

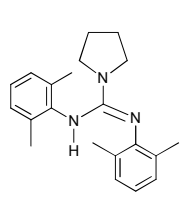
Analysis of the carbon nitrogen bond distances for compounds **1a, 22a & 27a** distinguishes the C=N imine from the C–N amine bonds, 1.288, 1.2810 and 1.2734; 1.365, 1.3805 and 1.3966 Å respectively, are very much close to the typical C=N and C–N bond distances {(1.28 (C=N) and 1.38 (C–N) Å)}. Sol-

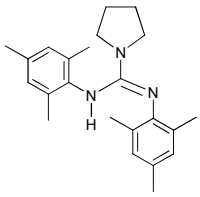
id state structures for both compounds **1a, 22a** exhibit in Z_{anti} conformation, where the central carbon atom is surrounded by three nitrogen atoms in a planar arrangement. It is found that the nitrogen atom part of cyclic secondary amine is in perpendicular to the N=C=N core of the carbodiimide moiety. And also, X-ray crystal structure for biguanidine (**27a**) reveals in Z_{anti}-Z_{anti} conformation.

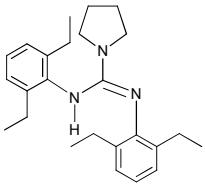
Further, we explored the possibility of catalyst free addition of aromatic primary and acylic secondary amines to *N,N'*-diaryl substituted carbodiimides to obtain tri- and tetra-substituted guanidines, respectively. The reaction between acyclic secondary amine and *N,N'*-diaryl substituted carbodiimide resulted in very poor yield at forced reaction conditions. However, addition of aromatic amine to *N,N'*-diaryl substituted carbodiimide failed to produce expected tri-substituted guanidine product, even at reflux temperature either in hydrocarbon or ethereal solvents. This is due to the decreased nucleophilicity of aromatic amines in comparison to cyclic secondary amines.

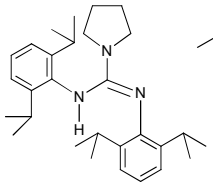
Table 1. Addition of cyclic secondary amines to symmetrical aryl carbodiimides[a,b]

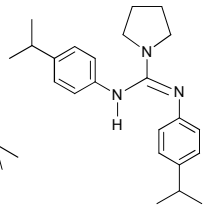


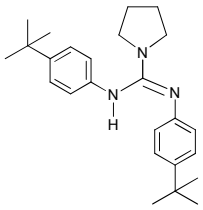

1a, 1h, 99%

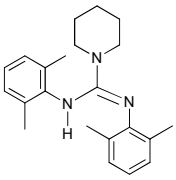

2a, 1.33h, 86%

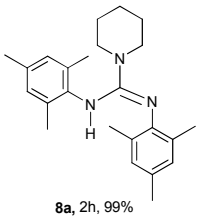

3a, 1.5h, 86%

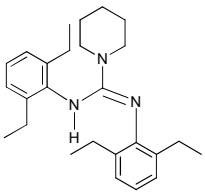

4a, 2h, 99%

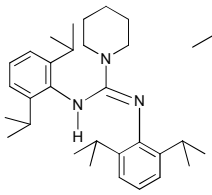

5a, 1.16h, 84%

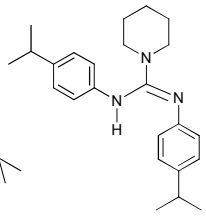

6a, 1h, 96%

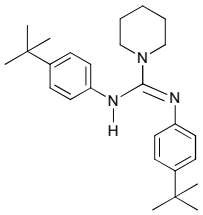

7a, 2h, 97%

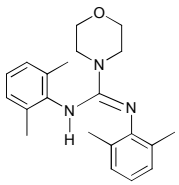

8a, 2h, 99%

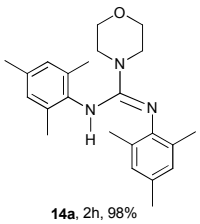

9a, 2h, 99%

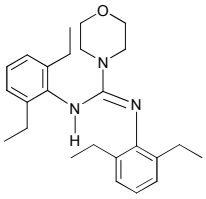

10a, 2h, 99%

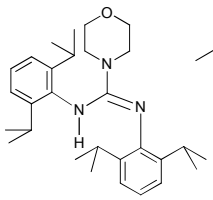

11a, 1h, 77%

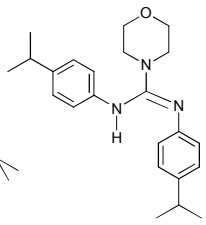

12a, 1h, 89%

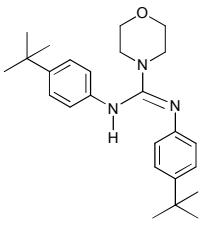

13a, 1.83h, 99%

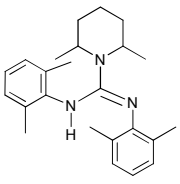

14a, 2h, 98%

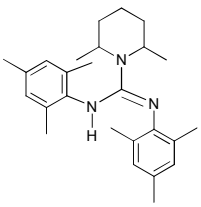

15a, 2h, 89%

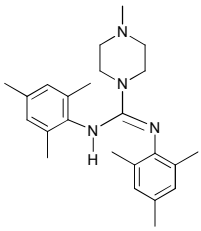

16a, 2h, 99%

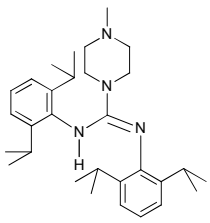

17a, 2h, 99%

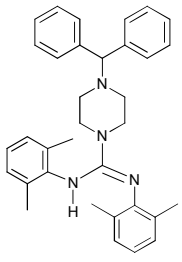

18a, 2h, 99%

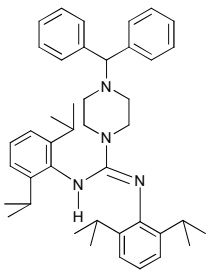

19a, 80°C, 24h, 42%


20a, 80°C, 24h, 37%


21a, 1h, 92%

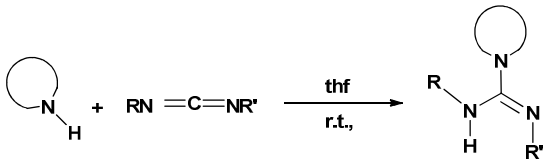

22a, 60°C, 2h, 89%


23a, 12h, 86%

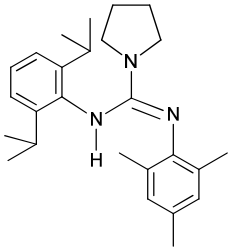

24a, 24h, 76%

[a]Unless otherwise mentioned all reactions were performed at room temperature.[b]Isolated yield

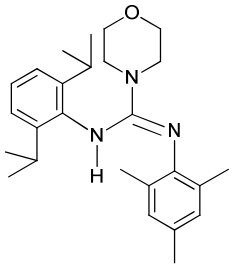
Table 2. Addition of cyclic secondary amines to unsymmetrical aryl carbodiimides[a]



25a & 26a



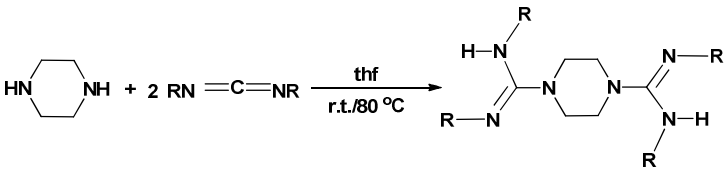
25a, 2h, 99%



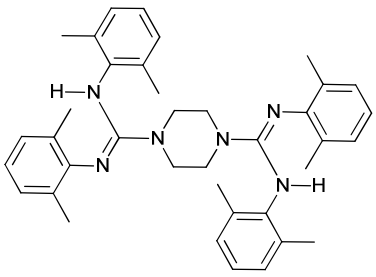
26a, 2h, 93%

[a]Isolated yield

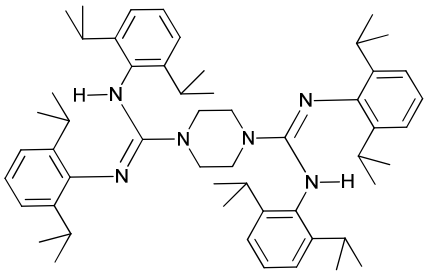
Table 3. Synthesis of bulky aryl biguanidines[a]



27a & 28a



27a, r.t., 4h, 90%



28a, 80°C, 12h, 60%

[a]Isolated yield

Conclusions

In conclusion, we have developed a straightforward and an atom economical, catalyst free C–N bond formation in guanylation reaction by the addition of cyclic secondary amines to various bulky aryl symmetrical and unsymmetrical carbodiimides to afford tetra-substituted guanidines in quantitative yields at ambient reaction conditions. These sterically and/or electronically stabilizing bulky acyclic guanidines may serve as important precursors to synthesize unusual metal complexes, particularly, low valent and/or low oxidation state main group, transition and lanthanide metal complexes. Further, direct addition of diamine to symmetrical aryl carbodiimides (2 equiv.) led to the formation of biguanidines, which are ideal precursors to construct dinuclear metal complexes.

Experimental

General considerations: All reactions were performed under an open atmosphere. Secondary amines were purchased from Spectrochem and distilled prior to use. All reaction mixtures were stirred magnetically and progress of the reactions were monitored by thin layer chromatography (TLC), using silica gel pre-coated plates. ^{1}H NMR (400 MHz) and ^{13}C{^{1}H} NMR (100 MHz) spectra were recorded on Bruker AV 400 NMR spectrometer. Deuterated chloroform ($CDCl_3$) and deuterated dichloromethane (CD_2Cl_2) were used as solvent for NMR spectra measurement. The chemical shift values (δ) were reported in parts per million (ppm) relative to the residual signals of solvents (δ 7.26, 5.32 for ^{1}H and δ 77.16, 53.84 for ^{13}C; for $CDCl_3$ and CD_2Cl_2 respectively). IR spectra were recorded on Perkin-Elmer FT-IR spectrometer. High Resolution Mass Spectra (HRMS) were recorded on BrukermicrOTOF-Q II Spectrometer. Melting points were taken on an electro thermal apparatus and are uncorrected.

General synthetic procedure: Synthesis of guanidines by the reaction of cyclic secondary amines and aromatic carbodiimides. A 50 mL round bottom flask was charged with secondary amines (1.02 mmol) and aromatic carbodiimides (1 mmol, (for biguanidine 2 mmol)), to that added tetrahydrofuran (5 mL). The reaction mixture was stirred at room temperature (few cases reflux temperature) for the required time and progress of the reaction was monitored by TLC. After completion of the reaction, it was extracted with dichloromethane, then pumped down the dichloromethane and dried to get crude compound. The crude residue was recrystallized from diethyl ether or hexane to give analytically pure compound. The synthesized compounds were fully characterized by ^{1}H, ^{13}C NMR, IR, and ESI-HRMS analyses. Further compounds **1a**, **22a** & **27a** were confirmed by X-ray crystal structural analysis.

Note: Initially, few guanylation reactions were conducted in benzene solvent and products isolated in quantitative yields. Further, same reactions were performed in thf solvent, we noticed that there is no change in the yield; therefore all reactions reported in this paper were conducted in thf.

(Z)-N,N'-bis(2,6-dimethylphenyl)pyrrolidine-1-carboximidamide (1a). (yield: 317mg, 0.986mmol, 99%); m.p. 119 – 120 ^{o}C; ^{1}H NMR (400 MHz, CD_2Cl_2, 25 ^{o}C): δ 1.71 – 1.74 (m, 4H, CH_2CH_2), 2.23 (s, 12H, *o*-CH_3), 3.03 – 3.07 (m, 4H, NCH_2), 5.06 (br, 1H, N*H*), 6.87 – 7.0 (m, 6H, Ar*H*). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C): δ 18.87 (CH_3), 25.53 (CH_2CH_2), 47.67 (NCH_2), 122.0, 125.6, 128.3, 130.8, 134.8, 137.8, 147.0 (Ar*C*), 148.4 (N_3C). IR (KBr) ν = 3364s (N-H), 2942m, 1620m, 1587m, 1407m, 1345m, 1258m, 1215m, 1074m, 776m, 759m, 706m cm^{-1}. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{21}H_{27}N_3$ 322.2278; Found 322.2289.

(Z)-N,N'-bis(2,4,6-trimethylphenyl)pyrrolidine-1-carboximidamide (2a). (yield: 301mg, 0.861mmol, 86%); m.p. 133 – 134 ^{o}C; ^{1}H NMR (400 MHz, CD_2Cl_2, 25 ^{o}C): δ 1.70 – 1.73 (m, 4H, CH_2CH_2), 2.18 (s, 12H, *o*-CH_3), 2.21 (s, 6H, *p*-CH_3), 3.02 – 3.05 (m, 4H, NCH_2), 5.06 (br,1H, N*H*), 6.81 (br, 4H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$, 25 ^{o}C): δ 18.4, 18.9 (*o*-CH_3), 20.8 (*p*-CH_3), 25.5 (CH_2CH_2), 47.6 (NCH_2), 128.9, 130.5, 130.8, 134.7, 135.1, 144.4 (Ar*C*), 148.9 (N_3C). IR (KBr) ν (cm^{-}

[1]): 3341s (N-H), 2977m, 2919m, 2855s, 1621m, 1596s, 1477m, 1404m, 1393m, 1344m, 1258m, 1226s, 1185s, 1075m, 858m, 759m, 706m. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{23}H_{31}N_3$ 350.2591; Found 350.2615.

(Z)-N,N'-bis(2,6-diethylphenyl)pyrrolidine-1-carboximidamide (3a). (yield: 325mg, 0.860mmol, 86%); m.p. 98 – 100 °C; ^{1}H NMR (400 MHz, CD_2Cl_2, 25 °C,): δ 1.17 (br, 12H, CH_2CH_3), 1.68 – 1.72 (m, 4H, CH_2CH_2), 2.60 (br, 8H, CH_2CH_3), 3.03 – 3.06 (m, 4H, CH_2CH_2), 5.05 (1H, NH), 6.99 – 7.05 (m, 6H, ArH). ^{13}C{^{1}H} NMR (100 MHz, CD_2Cl_2, 25 °C): δ 14.3 (CH_2CH_3), 24.9 (CH_2CH_3), 25.8 (NCH_2CH_2), 48.0 (NCH_2CH_2), 122.2, 124.4, 126.2, 136.9, 139.9, 141.0 (ArC), 148.3 (N_3C). IR (KBr) ν (cm^{-1}): 3381s (N-H), 2964s, 2931s, 2871s, 1610s, 1583s, 1450m, 1422m, 1346s, 1261m, 1215m, 1079m, 808s, 766m, 706m. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{25}H_{35}N_3$ 378.2904; Found 378.2913.

(Z)-N,N'-bis(2,6-diisopropylphenyl)pyrrolidine-1-carboximidamide (4a). (yield: 427mg, 0.984mmol, 99%); m.p. 136 – 137 °C; ^{1}H NMR (400 MHz, CD_2Cl_2, 25 °C): δ = 1.03 – 1.27 (m, br, 24H, $CH(CH_3)_2$), 1.67 – 1.70 (m, 4H, CH_2CH_2), 3.0 – 3.03 (m, 4H, NCH_2CH_2), 3.21 – 3.32 (sept, J = 8.0 Hz, 4H, $CH(CH_3)_2$), 5.03 (s, 1H, NH), 6.96 – 7.10 (m, 6H, ArH). ^{13}C NMR (100 MHz, CD_2Cl_2, 25 °C): δ = 22.7, 24.4, 25.3, ($CH(CH_3)_2$), 25.7 (NCH_2CH_2), 28.7 ($CH(CH_3)_2$), 48.3 (NCH_2CH_2), 122.4, 123.2, 123.7, 127.4, 135.1, 141.0, 145.3, 146.5 (ArC), 148.6 (N_3C). IR (KBr) ν (cm^{-1}): 3386s (N-H), 2960m, 2869m, 1615m, 1584m, 1463m, 1412m, 1323m, 1257m, 1177m, 1111m, 859m, 762m, 713m. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{29}H_{43}N_3$ 434.3530; Found 434.3540.

(Z)-N,N'-bis(4-isopropylphenyl)pyrrolidine-1-carboximidamide (5a). (yield: 292mg, 0.835mmol, 84%); oily; ^{1}H NMR (400 MHz, CD_2Cl_2, 25 °C): δ 1.19 – 1.21 (d, J = 8.0 Hz, 12H, $(CH(CH_3)_2)$), 1.82 – 1.85 (m, 4H, CH_2CH_2), 2.79 – 2.84 (sept, J = 8.0 Hz, 2H, $CH(CH_3)_2$), 3.30 – 3.33 (m, 4H, NCH_2CH_2), 6.78 – 6.80 (d, J = 8.0 Hz, 4H, ArH), 7.07 – 7.09 (d, J = 8.0 Hz, 4H, ArH) . ^{13}C{^{1}H} NMR (100 MHz, CD_2Cl_2, 25 °C): δ 24.3 ($CH(CH_3)_2$), 25.7 ($CH(CH_3)_2$), 33.8 (NCH_2CH_2), 47.8 (NCH_2CH_2), 121.1,

127.4, 142.7 (Ar*C*), 149.7 (N_3C). IR (KBr) ν (cm^{-1}): 3373s (N-H), 2959m, 2869m, 1618m, 1597m, 1508m, 1397m, 1242m, 1053m, 829m. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{23}H_{31}N_3$ 350.2591; Found 350.2602.

(Z)-N,N'-bis(4-tert-butylphenyl)pyrrolidine-1-carboximidamide (6a). (yield: 362mg, 0.958mmol, 96%); m.p. 80 – 82 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C,): δ 1.27 (s, 18H, C(CH_3)$_3$), 1.84 (br, 4H, CH_2CH$_2$), 3.35 (br, 4H, NCH_2CH$_2$), 6.86 – 6.88 (d, *J* = 8.0 Hz, 4H, Ar*H*) 7.22 – 7.24 (d, *J* = 8.0 Hz, 4H, Ar*H*) ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 25.3 (NCH$_2$*C*H$_2$), 31.5 (C(*C*H$_3$)$_3$), 34.2 (*C*(CH$_3$)$_3$), 47.8 (N*C*H$_2$CH$_2$), 120.9, 126.1, 142.7, 145.1 (Ar*C*), 150.2 (N_3C). IR (KBr) ν (cm^{-1}): 3375s (N-H), 2962m, 2869m, 1619m, 1595m, 1515m, 1393m, 1260m, 1190m, 1112m, 1014m, 825m, 559m. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{25}H_{35}N_3$ 378.2904; Found 378.2910.

(Z)-N,N'-bis(2,6-dimethylphenyl)piperidine-1-carboximidamide (7a). (yield: 324mg, 0.965mmol, 97%); m.p. 137 – 139 °C; ^{1}H NMR (400 MHz, CD_2Cl_2, 25 °C): δ 1.31 – 1.36 (m, 4H, CH_2CH$_2$), 1.43 – 1.49 (m, 2H, CH$_2$CH_2), 2.2 (s, 12H, *o*-CH$_3$), 3.01 – 3.04 (m, 4H, NCH_2), 5.0 (s, 1H, N*H*), 6.82 – 7.02 (m, 6H, Ar*H*). ^{13}C NMR (100 MHz, CD_2Cl_2, 25 °C): δ 18.5, 19.2 (*o*-*C*H$_3$), 25.2 (CH$_2$*C*H$_2$), 26. 0 (*C*H$_2$CH$_2$), 48.8 (N*C*H$_2$), 122.2, 125.5, 128.7, 130.0, 134.4, 138.1, 147.3 (Ar*C*), 151.6 (N_3C). IR (KBr) ν (cm^{-1}): 3375s (N-H), 2943m, 2927m, 2826m, 1623m, 1586m, 1407m, 1345m, 1281m, 1206m, 1069m, 975m, 780m, 761m. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{22}H_{29}N_3$ 336.2434; Found 336.2448.

(Z)-N,N'-bis(2,4,6-trimethylphenyl)piperidine-1-carboximidamide (8a). (yield: 359mg, 0.988mmol, 99%); m.p. 56 – 60 °C; ^{1}H NMR (400 MHz, CD_2Cl_2, 25 °C): δ 1.31 – 1.36 (m, 4H, CH_2CH$_2$), 1.43 – 1.49 (m, 2H, CH$_2$CH_2), 2.18 (s, 12H, *o*-CH_3), 2.21 (s, 6H, *p*-CH_3), 3.0 – 3.02 (m, 4H, NCH_2), 4.94 (s, 1H, N*H*), 6.83 (br, 4H, Ar*H*) ppm. ^{13}C NMR (100 MHz, CD_2Cl_2, 25 °C): δ 18.3, 19.1 (*o*-*C*H$_3$), 20.8 (*p*-*C*H$_3$), 25.2 (*C*H$_2$CH$_2$), 26.0 (CH$_2$*C*H$_2$), 48.8 (N*C*H$_2$), 129.3, 129.4, 129.7, 131.2, 134.2, 135.1, 135.5,

144.6 (Ar*C*), 152.2 (N_3C). IR (KBr) ν (cm^{-1}): 3382s (N-H), 2933m, 2853m, 2166m, 1627m, 1603m, 1470m, 1393m, 1279m, 1256m, 1233m, 1212m, 1215m, 1072m, 975m, 852m. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{24}H_{33}N_3$ 364.2747; Found 364.2765 .

(Z)-N,N'-bis(2,6-diethylphenyl)piperidine-1-carboximidamide (9a). (yield: 386mg, 0.985mmol, 99%); m.p. 119 – 120 °C; ^{1}H NMR (400 MHz, CD_2Cl_2, 25 °C): δ 1.10 – 1.22 (overlapping dd (br), 12H, CH_2CH_3), 1.27 – 1.36 (m, 4H, CH_2CH_2), 1.44 – 1.46 (m, 2H, CH_2CH_2), 2.59 – 2.74 (m, br, 8H, CH_2CH_3), 2.98 – 3.01 (m, 4H, NCH_2), 5.03 (s, 1H, N*H*), 6.91 – 7.05 (m, 6H, Ar*H*) . ^{13}C NMR (100 MHz, CD_2Cl_2, 25 °C): δ 14.4 (CH_2CH_3), 24.7 (CH_2CH_3), 25.2 ($CH_2CH_2CH_2$), 26.0 (NCH_2CH_2), 48.8 (NCH_2CH_2), 122.5, 126.4, 126.6, 135.8, 136.7, 140.1 , 146.3 (Ar*C*), 151.6 (N_3C). IR (KBr) ν (cm^{-1}): 3387s (N-H), 2969m, 2940m, 1633m, 1586m, 1449m, 1392m, 1373m, 1280m, 1116m, 1070m, 1033m, 974m, 853m, 764m. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{26}H_{37}N_3$ 392.3060; Found 392.3072.

(Z)-N,N'-bis(2,6-diisopropylphenyl)piperidine-1-carboximidamide (10a). Known compound,[18] (yield: 442mg, 0.987mmol, 99%); m.p. 119 – 120 °C; ^{1}H NMR (400 MHz, CD_2Cl_2, 25 °C): δ 1.1 – 1.32 (br, 24H, $CH(CH_3)_2$), 1.38 – 1.42 (m, 4H, CH_2CH_2), 1.46 – 1.49 (m, 2H, CH_2CH_2), 2.97 – 3.00 (m, 4H, NCH_2CH_2), 3.16 – 3.21 (sept, *J* = 8.0 Hz, 4H, $CH(CH_3)_2$), 5.02 (s, 1H, N*H*), 6.96 – 7.16 (m, Ar*H*). ^{13}C{^{1}H} NMR (100 MHz, CD_2Cl_2, 25 °C): δ 22.3, 23.0 ($CH(CH_3)_2$), 24.3, 25.2 ($CH(CH_3)_2$), 25.4 (CH_2CH_2), 25.7 (NCH_2CH_2), 28.7 ($CH(CH_3)_2$), 49.0 (NCH_2CH_2), 122.7, 123.2, 124.0, 127.0, 134.8, 140.1, 145.1, 145.5 (Ar*C*), 151.4 (N_3C). IR (KBr) ν (cm^{-1}): 3393s (N-H), 2960m, 1629m, 1585m, 1407m, 1389m, 1111m, 1074m, 776m, 760m. ESI-MS: $[M + H]^+$ 448.7.

(Z)-N,N'-bis(4-isopropylphenyl)piperidine-1-carboximidamide, (11a). (yield: 281mg, 0.772mmol, 77%); oily; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 1.21 – 1.22 (d, *J* = 4.0 Hz, 12H, $CH(CH_3)_2$), 1.53 – 1.55 (m, 6H, $CH_2CH_2CH_2$), 2.79 – 2.89 (sept, *J* = 8.0 Hz, 2H, $CH(CH_3)_2$), 3.28 (m, 4H, NCH_2CH_2), 4.69 (1H, N*H*), 6.86 (d, *J* = 8.0 Hz, 4H, Ar*H*) 7.09 (d, *J* = 8.0 Hz, 4H, Ar*H*). ^{13}C NMR (100 MHz,

$CDCl_3$, 25 °C): δ 24.1 ($CH(CH_3)_2$), 24.7 (CH_2CH_2), 25.3 (NCH_2CH_2), 33.4 ($CH(CH_3)_2$), 47.8 (NCH_2CH_2), 120.7, 127.2, 142.8 (Ar*C*), 152.0, (N_3C). IR (KBr) ν (cm^{-1}): 3375s (N-H), 2959m, 1631m, 1579m, 1516m, 1447m, 1413m, 1287m, 1254m, 1121m, 825m, 549m. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{24}H_{33}N_3$ 364.2747; Found 364.2772.

(Z)-N,N'-bis(4-(tert-butyl)phenyl)piperidine-1-carboximidamide (12a). (yield: 347mg, 0.888mmol, 89%); oily; ^{1}H NMR (400 MHz, CD_2Cl_2, 25 °C): δ 1.28 (s, 18H, $C(CH_3)_2$), 1.53 – 1.59 (m, 6H, CH_2CH_2), 3.25 – 3.27 (m, 4H, NCH_2CH_2), 6.82 (br, 4H, Ar*H*) 7.23 – 7.25 (d, *J* = 8.0 Hz, 4H, Ar*H*) ppm. ^{13}C NMR (100 MHz, CD_2Cl_2, 25 °C): δ 24.7 (CH_2CH_2), 25.3 (NCH_2CH_2), 31.5 ($C(CH_3)_3$), 34.2 ($C(CH_3)_3$), 47.8 (NCH_2CH_2), 120.3, 126.0, 145.0 (Ar*C*), 151.9 (N_3C). IR (KBr) ν (cm^{-1}): 3382s (N-H), 2961m, 2859m, 1621m, 1515m, 1393m, 1269m, 1113m, 1072m, 978m, 825m, 837m, 824m, 548m. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{26}H_{37}N_3$ 392.3060; Found 392.3064.

(Z)-N,N'-bis(2,6-dimethylphenyl)morpholine-4-carboximidamide (13a). (yield: 333mg, 0.986mmol, 99%); m.p. 174 – 175 °C; ^{1}H NMR (400 MHz, CD_2Cl_2, 25 °C): δ 2.24 (s, 12H, *o*-CH_3), 3.04 – 3.06 (m, 4H, NCH_2), 3.45 – 3.47 (m, 4H, OCH_2), 5.08 (s, 1H, N*H*), 6.83 – 7.02 (m, 6H, Ar*H*) . ^{13}C NMR (100 MHz, CD_2Cl_2, 25 °C): δ 18.3 (CH_3), 19.2 (CH_3), 48.3 (NCH_2), 66.9 (OCH_2), 122.5, 126.1, 128.6, 128.9, 129.8, 134.5, 137.6, 146.7 (Ar*C*), 151.1 (N_3C). IR (KBr) ν (cm^{-1}): 3364s (N-H), 2942m, 1620m, 1587m, 1407m, 1345m, 1258m, 1215m, 1074m, 776m, 759m, 706m. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{21}H_{27}N_3O$ 338.2227; Found 338.2257.

(Z)-N,N'-bis(2,4,6-trimethylphenyl)morpholine-4-carboximidamide (14a). (yield: 357mg, 0.976mmol, 98%); m.p. 148 – 150 °C; ^{1}H NMR (400 MHz, CD_2Cl_2, 25 °C): δ 2.19 (s, 12H, *o*-CH_3), 2.22 (s, 6H, *p*-CH_3), 3.03 – 3.05 (m, 4H, NCH_2CH_2), 3.44 – 3.47 (m, 4H, OCH_2CH_2), 5.02 (s, 1H, N*H*), 6.82 – 6.86 (m, 4H, Ar*H*). ^{13}C NMR (100 MHz, CD_2Cl_2, 25 °C): δ 18.2 (*o*-CH_3), 19.1 (*o*-CH_3), 20.8 (*p*-CH_3), 48.3 (NCH_2), 66.9 (OCH_2), 129.3, 129.6, 131.5, 134.3, 135.0, 135.6, 144.1 (Ar*C*), 151.5 (N_3C).

IR (KBr) ν (cm^{-1}): 3364s (N-H), 2974m, 2917m, 2849m, 2373m, 1637m, 1458m, 1384m, 1305m, 1267m, 1113m, 1085m, 984m, 855m, 807s. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{23}H_{31}N_3O$ 366.2540; Found 366.2558.

(Z)-N,N'-bis(2,6-diethylphenyl)morpholine-4-carboximidamide (15a). Known compound,[27] (yield: 350mg, 0.889mmol, 89%); m.p. 144 – 147 °C; ^{1}H NMR (400 MHz, CD_2Cl_2, 25 °C): δ 1.09 – 1.12 (t, J = 8.0, 4.0 Hz, 6H, CH_2CH_3), 1.22 – 1.25 (t, J = 8.0, 4.0 Hz, 6H, CH_2CH_3), 2.50 – 2.78 (m, 8H, CH_2CH_3), 3.02 – 3.04 (m, 4H, NCH_2), 3.44 – 3.46 (m, 4H, OCH_2), 5.11 (s, 1H, NH), 6.91 – 7.09 (m, 6H, ArH). ^{13}C NMR (100 MHz, CD_2Cl_2, 25 °C): δ 14.3 (CH_2CH_3), 14.5 (CH_2CH_3), 24.7 (CH_2CH_3), 25.3 (CH_2CH_3), 48.3 (NCH_2), 66.8 (OCH_2), 122.8, 126.4, 126.6, 126.8, 135.6, 136.2, 140.3, 145.8 (ArC), 151.0 (N_3C). IR (KBr) ν (cm^{-1}): 3330s (N-H), 2969m, 2936m, 2858m, 2373m, 1638m, 1458m, 1381m, 1364m, 1273m, 1115m, 1084m, 982m, 855m, 809s. ESI-MS: $[M + H]^+$ 394.3.

(Z)-N,N'-bis(2,6-diisopropylphenyl)morpholine-4-carboximidamide (16a). (yield: 443mg, 0.985mmol, 99%); m.p. 134 – 135 °C; ^{1}H NMR (400 MHz, CD_2Cl_2, 25 °C): δ 0.99 (br, 6H, $CH(CH_3)_2$), 1.16 – 1.18 (d, J = 8.0 Hz, 6H, $CH(CH_3)_2$), 1.31 – 1.33 (d, J = 8.0 Hz, 12H, $CH(CH_3)_2$), 3.01 – 3.03 (m, 4H, NCH_2CH_2), 3.13 – 3.21 (sept, J = 8.0, 4.0 Hz, 4H, $CH(CH_3)_2$), 3.49 – 3.51 (m, 4H, OCH_2CH_2), 5.09 (s, 1H, NH), 6.96 – 7.20 (m, 6H, ArH). ^{13}C NMR (100 MHz, CD_2Cl_2, 25 °C): δ 22.3, 22.9 ($CH(CH_3)_2$), 24.3, 25.4 ($CH(CH_3)_2$), 28.8, 28.9 ($CH(CH_3)_2$, 48.6 (NCH_2CH_2), 66.6 (OCH_2CH_2), 123.0, 123.3, 124.2, 127.4, 134.2, 140.2, 144.5 , 145.6 (ArC), 150.9 (N_3C). IR (KBr) ν (cm^{-1}): 3354s (N-H), 2968m, 2936m, 2858m, 2373m, 1638m, 1458m, 1381m, 1364m, 1273m, 1115m, 1084m, 982m, 855m, 809s. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{29}H_{43}N_3O$ 450.3479; Found 450.3506.

(Z)-N,N'-bis(4-isopropylphenyl)morpholine-4-carboximidamide (17a). (yield: 360mg, 0.984mmol, 99%); oily; ^{1}H NMR (400 MHz, CD_2Cl_2, 25 °C): δ 1.20 – 1.21 (d, J = 4.0 Hz, 12H, $CH(CH_3)_2$), 2.78 - 2.89 (sept, J = 8.0 Hz, 2H, $CH(CH_3)_2$), 3.27 – 3.29 (m, 4H, NCH_2), 3.62 – 3.64 (m, 4H, OCH_2), 5.52 (br,

1H, N*H*), 6.80 – 7.11 (m, 8H, Ar*H*). ^{13}C NMR (100 MHz, CD_2Cl_2, 25 °C): δ 24.2 (CH(CH_3)$_2$), 33.8 (*C*H(CH_3)$_2$), 47.4(NCH_2), 66.7 (OCH_2), 119.0, 122.1, 127.5, 140.5, 143.2, 147.7 (Ar*C*), 151.4 (N_3*C*). IR (KBr) ν (cm^{-1}): 3330s (N-H), 2969m, 2936m, 2858m, 2373m, 1638m, 1458m, 1381m, 1364m, 1273m, 1115m, 1084m, 982m, 855m, 809s. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{23}H_{31}N_3O$ 366.2540; Found 366.2543.

(Z)-N,N'-bis(4-tert-butylphenyl)morpholine-4-carboximidamide (18a). (yield: 390mg, 0.990mmol, 99%); m.p. 126 – 127 °C; ^{1}H NMR (400 MHz, CD_2Cl_2, 25 °C): δ 1.28 (s, 18H, C(CH_3)$_3$), 3.27 – 3.30 (m, 4H, NCH_2CH_2), 3.63 – 3.65 (m, 4H, OCH_2CH_2), 5.52 (br, 1H, N*H*), 6.78 – 7.27 (m, 8H, Ar*H*). ^{13}C NMR (100 MHz, CD_2Cl_2, 25 °C): δ 31.6 (C(*C*H$_3$)$_3$), 34.4 (*C*(CH$_3$)$_3$), 47.4 (N*C*H$_2$), 66.7 (O*C*H$_2$), 118.6, 121.9, 126.5, 139.8, 145.4, 147.4, (Ar*C*), 151.4 (N_3*C*). IR (KBr) ν (cm^{-1}): 3382m (N-H), 3249m, 3162m, 2958m, 1627m, 1575m, 1513s, 1446s, 1427s, 1360m, 1364m, 1273m, 1115m, 1084m, 982m, 855m, 809s. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{25}H_{35}N_3O$ 394.2853; Found 394.2872.

(Z)-N,N'-bis(2,6-dimethylphenyl)-2,6-dimethylpiperidine-1-carboximidamide (19a). (yield: 154mg, 0.423mmol, 42%); oily; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 1.26 (d, 6H, *J* = 8.0 Hz, C*H*$_3$), 1.35 – 1.85 (m, 6H, CH$_2$C*H*$_2$), 2.24 (s, 6H, *o*-C*H*$_3$), 2.29 (s, 6H, *o*-C*H*$_3$), 3.90 – 3.97 (m, 2H, NC*H*), 4.98 (s, 1H, N*H*), 6.82 – 7.03 (m, 6H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 14.5 (CH$_2$*C*H$_2$CH$_2$), 18.5, 19.07 (*o*-*C*H$_3$), 20.9 (NCH*C*H$_3$), 30.3 (CH*C*H$_2$CH$_2$), 48.1 (N*C*H), 121.9, 125.2, 128.4, 128.7, 129.3, 133.7, 138.5, 147.5 (Ar*C*), 150.4 (N_3*C*). IR (KBr) ν (cm^{-1}): 3373s (N-H), 2930m, 1619m, 1587m, 1469m, 1405m, 1367m, 1212m, 1148m, 1117m, 1037m, 974m, 894m, 774m, 766m. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{24}H_{33}N_3$ 364.2747; Found 364.2767.

(Z)-N,N'-bis(2,4,6-trimethylphenyl)-2,6-dimethylpiperidine-1-carboximidamide (20a). (yield: 147mg, 0.374mmol, 37%); m.p. 69 – 72 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 1.25 (d, 6H, *J* = 8.0 Hz, C*H*$_3$), 1.35 – 1.85 (m, 6H,C*H*$_2$C*H*$_2$C*H*$_2$), 2.19 – 2.24 (m, 18H, *o,p*-C*H*$_3$), 3.91 – 3.97 (m, 2H, NC*H*),

4.94 (s, 1H, N*H*), 6.79 – 6.85 (m, 4H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$, 25 ^{o}C): δ 14.6 ($CH_2CH_2CH_2$), 18.5, 18.9 (*o*-CH_3), 20.8 (*p*-CH_3), 20.9 ($NCHCH_3$), 30.3 ($CHCH_2CH_2$), 47.99 (N*C*H), 129.1, 129.3, 129.7, 130.8, 133.7, 134.6, 135.8, 144.8 (Ar*C*), 150.9 (N_3C). IR (KBr) ν (cm^{-1}): 3375s (N-H), 2931m, 1621m, 1600m, 1478m, 1404m, 1368m, 1219m, 1146m, 1119m, 1036m, 888m, 852m. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{26}H_{37}N_3$ 392.3060; Found 392.3086.

(Z)-N,N'- bis(2,4,6-trimethylphenyl)-4-methylpiperazine-1-carboximidamide (21a). (yield: 348mg, 0.919mmol, 92%); m.p. 129 – 131 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C): δ 2.17 (s, 6H, *o*-CH_3), 2.22 – 2.23 (m, 19H, *o*-CH_3, NCH_3, CH_3NCH_2), 3.12 (br, 4H, NCH_2), 5.00 (1H, N*H*), 6.80 (s, 2H, Ar*H*), 6.85 (s, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$, 25 ^{o}C): δ 18.2, 19.1 (*o*-CH_3), 20.8, 20.9 (*p*-CH_3), 46.2 (NCH_3), 47.2 (NCH_2), 54.9 (CH_3NCH_2), 129.1, 129.4, 129.7, 131.4, 133.8, 134.7, 135.2, 143.6, (Ar*C*), 151.5 (N_3C). IR (KBr) ν (cm^{-1}): 3317m (N-H), 2915m, 2852m, 2797m, 1629m, 1600m, 1396m, 1368m, 1297m, 1266m, 1233m, 1214m, 1136m, 1006m, 989m, 857m,546s. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{24}H_{34}N_4$ 379.2856; Found 379.2870.

(Z)-N,N'-bis(2,6-diisopropylphenyl)-4-methylpiperazine-1-carboximidamide (22a). (yield: 413mg, 0.892mmol, 89%); m.p. 147 – 149 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C): δ 0.99 – 1.32 (br, dd, 24H, $CH(CH_3)_2$), 2.22 (s, 3H, NCH_3), 2.29 (br, 4H, NCH_2), 3.09 (br, 4H, CH_3NCH_2), 3.13 – 3.20 (sept, *J* = 8.0 Hz, 4H, C*H*(CH_3)$_2$), 5.05 (s, 1H, N*H*), 7.0 – 7.14 (m, 6H, Ar*H*) ^{13}C NMR (100 MHz, $CDCl_3$, 25 ^{o}C): δ 22.3, 22.9, 24.2, 25.3 ($CH(CH_3)_2$), 28.5, 28.6 ($CH(CH_3)_2$), 46.3 (NCH_3), 47.5 (NCH_2), 54.5 (CH_3NCH_2), 122.8, 123.0, 123.9, 126.9, 134.0, 139.7, 144.3, 145.0 (Ar*C*), 150.4 (N_3C). IR (KBr) ν (cm^{-1}): 3391s (N-H), 2959m, 2841m, 2795s, 1626m, 1586m, 1394m, 1368m, 1267m, 1145m, 1079m, 989m, 805m, 762m. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{30}H_{46}N_4$ 463.3795; Found 463.3807.

(Z)-4-benzhydryl-N,N'-bis(2,6-dimethylphenyl)piperazine-1-carboximidamide (23a). (yield: 420mg, 0.858mmol, 86%); m.p. 174 – 177 °C; ^{1}H NMR (400 MHz, CD_2Cl_2, 25 °C): δ 2.20 (s, 10H, C*H*$_3$(6H), NC*H*$_2$(4H)), 2.26 (s, 6H, C*H*$_3$), 3.11 – 3.13 (m, 4H, NC*H*$_2$), 4.12 (s, 1H, C*H*(Ph)$_2$), 5.02 (s, 1H, N*H*), 6.83 – 7.05 (m, 6H, Ar*H*), 7.15 (m, 2H, Ar*H*), 7.24 (m, 4H, Ar*H*), 7.38 (m, 4H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 18.2, 19.1 (*C*H$_3$), 47.4 (N*C*H$_2$), 51.8 (CHN*C*H$_2$), 76.3 (Ph$_2$*C*H), 122.4, 125.7, 127.0, 127.9, 128.4, 128.6, 128.7, 129.8, 133.9, 137.3, 142.8, 146.4 (Ar*C*), 151.1 (N$_3$*C*). IR (KBr) ν (cm^{-1}): 3364s (N-H), 3027m, 2968m, 2915s, 2848s, 2821m, 1637m, 1587m, 1469m, 1451m, 1396m, 1305m, 1257m, 1214m, 1126m, 1080m, 991m, 784m, 764m, 705m. HRMS (ESI/TOF-Q) m/z: [M + H]$^+$ Calcd for $C_{34}H_{38}N_4$ 503.3169; Found 503.3159.

(Z)-4-benzhydryl-N,N'-bis(2,6-diisopropylphenyl)piperazine-1-carboximidamide (24a). (yield: 465mg, 0.756mmol, 76%); m.p. 154 – 157 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 0.97 – 1.31 (d, 24H, CH(C*H*$_3$)$_2$), 2.25 (m, 4H, CHNC*H*$_2$), 3.06 – 3.08 (m, 4H, NC*H*$_2$), 3.12 – 3.18 (sept, 4H, C*H*(CH$_3$)$_2$), 4.10 (s, 1H, C*H*(Ph)$_2$), 5.02 (s, 1H, N*H*),), 6.97 – 7.05 (m, 3H, Ar*H*), 7.10 – 7.16 (m, 5H, Ar*H*), 7.22 – 7.26 (m, 4H, Ar*H*), 7.38 – 7.39 (m, 4H, Ar*H*). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 22.2, 22.9, 24.2, 25.4 (CH(*C*H$_3$)$_2$), 28.4, 28.5 (*C*H(CH$_3$)$_2$), 47.9 (N*C*H$_2$), 51.6 (*C*HNCH$_2$), 76.6 (N*C*H), 122.5, 123.0, 123.7, 126.8, 127.0, 127.9, 128.6, 134.0, 139.7, 142.9, 144.4, 145.0 (ArC), 150.7 (N$_3$*C*). IR (KBr) ν (cm^{-1}): 3394s (N-H), 2960m, 2925m, 1582s, 1450m, 1423m, 1302m, 1138m, 977m, 805m, 706m. HRMS (ESI/TOF-Q) m/z: [M + H]$^+$ Calcd for $C_{42}H_{54}N_4$ 615.4421; Found 615.4417.

(Z)-N'-(2,6-diisopropylphenyl)-N-(2,4,6-trimethylphenyl)pyrrolidine-1-carboximidamide (25a). (yield: 386mg, 0.985mmol, 99%); m.p. 120 – 123 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 1.03 – 1.26 (m, 12H, CH(C*H*$_3$)$_2$), 1.72 (b, 4H, CH$_2$C*H*$_2$), 2.18 – 2.22 (br, 9H, *o,p*-C*H*$_3$), 3.06 (br, 4H, NC*H*$_2$), 3.30 (br, 2H, C*H*(CH$_3$)$_2$), 5.09 (br, 1H, N*H*), 6.80 – 7.15 (m, 5H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 18.1, 19.0 (o-*C*H$_3$), 20.8 (*p*-*C*H$_3$), 22.4, 23.3, 24.4, 24.7 (CH(*C*H$_3$)$_2$), 25.5 (NCH$_2$*C*H$_2$), 28.09, 28.2 (CH(*C*H$_3$)$_2$), 47.8 (N*C*H$_2$CH$_2$), 122.4, 123.2, 123.4, 127.1, 129.1, 130.7, 134.4, 135.0, 141.2, 146.0

(Ar*C*), 148.2 (N_3C). IR (KBr) ν (cm^{-1}): 3380s (N-H), 2960m, 2924m, 2876m, 1610m, 1584m, 1489m, 1418m, 1412m, 1231m, 1078m, 861m, 713m. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{26}H_{37}N_3$ 392.3060; Found 392.3072.

(Z)-N'-(2,6-diisopropylphenyl)-N-(2,4,6-trimethylphenyl)morpholine-4-carboximidamide (26a). (yield: 381mg, 0.934mmol, 93%); m.p. 131 – 133 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 1.01 – 1.29 (m, 12H, $CH(CH_3)_2$), 2.18 – 2.22 (2s, 9H, *o*-CH_3(6H), *p*-CH_3(3H)), 3.09 – 3.10 (m, 4H, NCH_2), 3.14 – 3.24 (sept, 2H, $CH(CH_3)_2$), 3.51 – 3.54 (m, 4H, OCH_2), 4.98, 5.10 (s, 1H, N*H*), 6.81 – 6.87 (2s, 2H, Ar*H*), 6.99 – 7.03 (m, 1H, Ar*H*), 7.08 – 7.17 (m, 2H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 17.9, 19.1 (*o*-CH_3), 20.8 (*p*-CH_3), 22.5, 22.9 ($CH(CH_3)_2$), 24.3, 24.8 ($CH(CH_3)_2$), 28.1, 28.5 ($CH(CH_3)_2$), 47.9, 48.1 (NCH_2), 66.5, 66.8 (OCH_2), 122.9, 123.3, 123.8, 127.2, 129.2, 129.6, 131.6, 133.6, 134.1, 134.4, 135.0, 135.2, 140.0, 143.3, 143.8, 145.1 (Ar*C*) 150.6, 152.0 (N_3C). IR (KBr) ν (cm^{-1}): 3369s (N-H), 2963m, 2856m, 1621m, 1583m, 1486s, 1456s, 1399s, 1365s, 1231m, 1113s, 986m, 853m. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{26}H_{37}N_3O$ 352.5468; Found 352.5465.

(1Z,4Z)-N1,N'1,N4,N'4-tetrakis(2,6-dimethylphenyl)piperazine-1,4-bis(carboximidamide) (27a). (yield: 527mg, 0.898mmol, 90%); m.p. 246 – 249 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 2.2 (s, 12H, *o*-CH_3), 2.24 (s, 12H, *o*-CH_3), 2.94 (br, 8H, NCH_2), 5.03 (s, 2H, N*H*), 6.83 – 7.05 (m, 12H, Ar*H*). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 18.2, 19.1 (CH_3), 47.1 (NCH_2), 122.5, 126.0, 128.4, 128.8, 129.7, 133.9, 137.0, 146.1 (Ar*C*), 151.1 (N_3C). IR (KBr) ν (cm^{-1}): 3376s (N-H), 2916s, 2848s, 1628m, 1588m, 1471m, 1395m, 1248m, 1290m, 1211m, 1085m, 989m, 778m,767s. HRMS (ESI/TOF-Q) m/z: $[M + H]^+$ Calcd for $C_{38}H_{46}N_6$ 587.3857; Found 587.3842.

(1Z,4Z)-N1,N'1,N4,N'4-tetrakis(2,6-diisopropylphenyl)piperazine-1,4-bis(carboximidamide) (28a). Known compound,[17] (yield: 485mg, 0.597mmol, 60%); m.p. 200 – 202 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 0.98 – 1.30 (m, 48H, $CH(CH_3)_2$), 2.97 (s, 8H, NCH_2), 3.09 – 3.14 (sept, *J* = 8.0 Hz, 8H,

C*H*$(CH_3)_2$), 5.03 (s, 2H, N*H*), 6.97 – 7.18 (m, 12H, Ar*H*) ^{13}C NMR (100 MHz, $CDCl_3$, 25 ^oC,): δ 22.5, 23.0 (CH(*C*$H_3)_2$, 24.2, 25.4 (CH(*C*$H_3)_2$, 28.4, 28.5 (*C*H$(CH_3)_2$, 46.9 (N*C*H_2CH_2), 122.7, 123.0, 123.9, 127.0, 133.8, 139.8, 144.1, 144.9 (Ar*C*), 150.5 (N_3C). IR (KBr) ν (cm^{-1}): 3391s (N-H), 2962m, 2868m, 2373m, 1623m, 1400m, 1384m, 1342m, 1326m, 1290m, 1259m, 1115m, 1084m, 990m, 758m. ESI-MS: $[M + H]^+$ 811.6.

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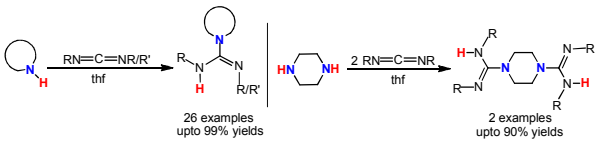
Table of Contents

Metal free guanylation reaction of cyclic secondary amines with bulky aryl carbodiimides



Catalyst free direct addition of cyclic secondary amines to various *N,N*'-bisaryl substituted carbodiimdes led to the formation of bulky guanidines. Further, two equivalents of *N,N*'-bisaryl substituted carbodiimides upon treatement with piperazine led to the formation of bis guanidines.

Keywords: Amine, Carbodiimide, C–N bond formation, Guanidine, N–H bond activation