ChemPubSoc Europe

DOI: 10.1002/chem.201702270

CHEMISTRY A European Journal Full Paper

Reaction Mechanisms

Copper-Assisted Amination of Boronic Acids for Synthesis of Bulky Diarylamines: Experimental and DFT Study

Oleg A. Levitskiy, Yuri K. Grishin, Vyacheslav V. Sentyurin, and Tatiana V. Magdesieva*[a]

Abstract: Comparative investigation of copper-assisted oxidative and reductive amination showed that the latter was preferable for the synthesis of bulky diarylamines. DFT estimation of the mechanism of copper(I)-assisted reductive amination of boronic acids with aryl nitroso compounds was performed and possible active species were identified. DFT estimation of the steric penalty revealed that the barrier for the transmetalation step for the hindered nitroso compound was almost the same as that for the unsubstituted one, whereas a bulky group in the boronic acid increased the activation energy. A DFT study of the influence of the electronic properties of the substituents in both reactants on the activation energy revealed that the optimal combination for the synthesis of unsymmetrical diarylamines to provide better yields was an electron-rich aryl boronic acid and an electron-deficient nitroso compound. By using these helpful guidelines, a series of new bulky diarylamines were obtained and fully characterized.

Introduction

Diarylamines constitute an important family of organic compounds that are widely used in pharmaceutical, biological, and materials sciences.[1] The diarylamino functionality is present in a wide range of natural products[2] and as ligands in metal complexes.[3] Although a variety of methods have been developed for the formation of diarylamines, they cannot be considered as universally efficient in each case, for each type and location of substituent in the aromatic ring. Among other compounds, the synthesis of *ortho*-substituted aryl derivatives is an especially tricky task due to the additional contribution of steric demands. Meanwhile, bulky diarylamines are of interest as possible precursors for the corresponding stable diaryl nitroxides, which have the potential for various practical applications, for example, as structurally tunable redox-active materials.[4] Diarylnitroxides can be obtained through the oxidation of diarylamines by using H_2O_2/Na_2WO_4 or *m*-chloroperbenzoic acid.[5,6] At present, only a few stable diarylnitroxides are known, and all of them are *para*-substituted derivatives to prevent further chemical transformations of the radicals that are possible due to spin delocalization over the phenyl rings. This substantially limits the scope of stable radicals available. An alternative route to the stabilization of the radical might be insertion of a bulky substituent into the *ortho* position, which will force the aryl ring to twist away from the N–O plane; thus disturbing its conjugation to the radical center.[7] Therefore, the search for convenient, efficient, and relatively cheap methods for the preparation of bulky *ortho*-substituted diarylamines as precursors for stable nitroxides is a challenging task, and the systematic investigation of the influence of the location of substituents on the peculiarities of the synthetic procedure may provide guidelines for selecting an optimal route.

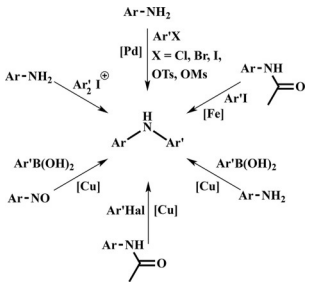
Recent efforts in the formation of diarylamine functional groups mainly focused on transition-metal-catalyzed cross-coupling of anilines with other aromatic compounds (for reviews, see refs. [8], [9]). These are well-established and straightforward methods. In spite of the availability of the main mechanistic guidelines and a huge amount of experimental data that have been already obtained, the best choice of catalyst and reaction conditions for each particular combination of reactants is still a state-of-the-art issue. Catalytic amination of aromatic compounds is commonly most efficient if precious metals are used, typically, in the form of complexes with complicated phosphine ligands. Recently, trineopentylphosphine was suggested for the coupling of sterically demanding substrates in Buchwald–Hartwig amination and showed high efficiency.[10] It was demonstrated that the conformational flexibility of the ligand plays a key role in allowing the palladium catalyst to couple hindered substrates (e.g., 2,6-diisopropyl aniline; the combination of two reactants with more bulky *ortho tert*-butylphenyl moieties has not been explored[10]). However, phosphine ligands (as well as palladium) are expensive and toxic, and a high reaction temperature is required.

Among alternative methods recently described, arylation of anilines with diaryliodonium salts[11] and iron-catalyzed N-arylation of acetanilides[12] should be mentioned (Scheme 1).

Because further practical application of diarylamines and corresponding nitroxides requires the development of synthetic approaches that avoid precious metals, expensive and com-

[a] Dr. O. A. Levitskiy, Y. K. Grishin, V. V. Sentyurin, Prof. Dr. T. V. Magdesieva
Lomonosov Moscow State University, Chemistry Dept.
Leninskie Gory 1/3, Moscow 119991 (Russia)
E-mail: tvm@org.chem.msu.ru

Supporting information for this article can be found under: https://doi.org/10.1002/chem.201702270. It contains HRMS and ^{1}H, ^{19}F, and ^{13}C NMR spectra; HMBC and HSQC 2D NMR data; and details of DFT calculations.



Scheme 1. Synthetic routes to diarylamines. Ts = tosyl, Ms = mesyl, Hal = halogen.

plicated ligands, or reactive organometallic reagents, copper-assisted oxidative and reductive amination of aryl boronic acids seems to be the most practical alternative to traditional Buchwald–Hartwig amination. Notably, Buchwald and Antilla emphasized the significance of this practical approach.[13] Both oxidative and reductive copper-assisted amination of aryl boronic acids with arylamines or nitrosoarenes, respectively, have been suggested previously.[14–17] Oxidative amination (the Chan–Lam method) has been widely used for the synthesis of various diarylamines (see ref. [18], and references cited therein); reductive amination of aryl boronic acids has attracted significantly less attention in the literature: to the best of our knowledge, only one paper on the subject has been published.[15] It was demonstrated that the presence of even a methyl group in the *ortho* position to boron had a dramatic influence on the oxidative coupling reaction rate,[13] but a systematic investigation of the influence of a bulky group in the *ortho* and *para* positions in the aryl boronic acid or in the N-containing component (nitroso compound or amine) on the applicability of the methods has not yet been performed. Moreover, it was mentioned in a recent review that the copper-catalyzed Chan–Lam method was unsuitable for the preparation of hindered anilines.[19]

Herein, we aim to report a comparative investigation of the efficiency of copper-assisted oxidative and reductive aminations for the synthesis of a series of bulky diarylamines with *ortho*-/*para*-*tert*-butyl and trifluoromethyl substituents on the aromatic rings. To the best of our knowledge, the compounds have not been obtained previously (except symmetrical 4,4′-bis(*tert*-butyl-[20–22]). Amination of isomeric *ortho*-/*para*-*tert*-butylphenyl boronic acids with *ortho*-/*para*-*tert*-butylphenylamines or *tert*-butylnitrosobenzenes is discussed to reveal the preferential nature of the N-component (amine or nitroso compound) and the optimal combination of the location of bulky substituents in the reactants (boron or N-component) to provide a better yield of unsymmetrical diarylamine. Based on the results obtained, the synthesis of a series of bulky *ortho*-*tert*-butyl- and trifluoromethyl-containing diarylamines is presented.

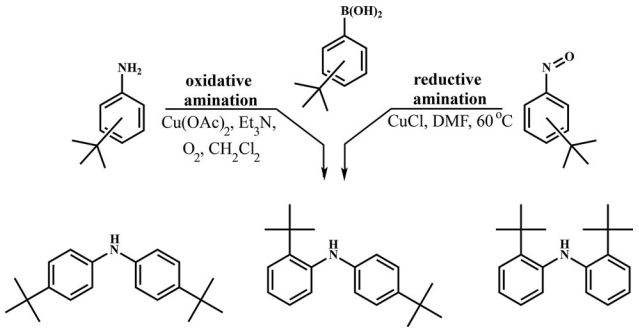
Because data on the reaction mechanisms are scarce, results of the computational DFT evaluation of possible mechanisms of copper(I)-mediated reductive amination of the aryl boronic acid with an aryl nitroso compound is discussed. Detailed potential energy profiles for feasible reaction paths, as well as possible active species, are examined. DFT estimation of the influence of electronic and steric properties of the substituents in both reactants on the rate-determining step provide guidelines for choosing an optimal synthetic procedure, leading to unsymmetrical diarylamines.

The selection of the substituents (bulky *t*Bu and CF_3 groups in various combinations) allows an estimation of the influence of the electronic properties of the substituents on the reaction yield. New sterically hindered symmetrical and unsymmetrical *tert*-butyl- and trifluoromethyl-substituted diphenylamines are of interest as the precursors for the corresponding diarylnitroxides, which are good candidates for testing the idea of diarylnitroxides stabilization through breaking conjugation between the aromatic ring and NO radical center.[7] The stability of the corresponding nitroxides further obtained from the diarylamine precursors through oxidation imposes some additional restrictions: sterically demanding substituents without α-hydrogen atoms are required.[23]

Results and Discussion

Oxidative versus reductive amination of *tert*-butylphenyl boronic acids

To evaluate the comparative efficiency of the oxidative and reductive copper-assisted amination of aryl boronic acids, the interaction of the *ortho*- and *para*-*tert*-butylphenyl boronic acids with *ortho*/*para tert*-butylphenyl amines and *ortho*/*para tert*-butylphenyl nitrosobenzenes was investigated. Oxidative amination was studied first. The *ortho*- and *para*-*tert*-butylphenyl boronic acids were synthesized according to a previously described procedure.[24] Oxidative amination was carried out by using an equimolar amount of $Cu(OAc)_2$ in the presence of a tertiary amine in dichloromethane at room temperature (Scheme 2).



Scheme 2. Oxidative and reductive amination of *tert*-butylphenyl boronic acids.

To optimize the reaction protocol, both *para*-*tert*-butyl-substituted reactants were taken as the simplest case. This allowed us to obtain 4,4′-bis(*tert*-butylphenyl)amine in 65% yield. Contrary to the other compounds discussed herein, 4,4′-bis(*tert*-butylphenyl)amine was previously reported.[20] It was obtained in a similar yield by means of palladium-catalyzed cross-coupling[21] and alkylation of diphenylamine on the zeolite catalyst.[22]

Encouraged with this result, we turned to the *ortho* derivatives. First, *ortho*-*tert*-butylaniline was involved in the reaction with *para*-*tert*-butylphenyl boronic acid. 2,4′-Bis(*tert*-butylphenyl)amine was isolated in 22% yield; a certain amount of *tert*-butylbenzene was also found in the reaction mixture. Attempts to improve the reaction yield by increasing the reaction time were performed, but did not lead to better results.

The unsymmetrical 2,4′-bis(*tert*-butylphenyl)amine was obtained as white crystals with a melting point of 86–88 °C and completely characterized by spectral methods. ESI-HRMS data supported that the reaction product was the target amine; the signal of the molecular ion and a characteristic isotopic distribution were observed. The ^{1}H and ^{13}C NMR spectra support the structure of the target compound (see the Experimental Section and Supporting Information).

An alternative combination (*ortho*-*tert*-butylphenyl boronic acid and *para*-*tert*-butyl aniline) was not successful; the target diarylamine was isolated in only 7% yield.

The obtained result made it senseless to attempt to synthesize the most sterically demanding symmetrical 2,2′-bis(*tert*-butylphenyl)amine by using this approach and we turned our attention to reductive amination.

In this case, aryl boronic acids and nitroso aromatic compounds were used; C–N bond formation is promoted by a stoichiometric amount of CuCl, which serves as a catalyst and reducing agent.[15] The method utilizes cheap reactants and provides good yields of unsymmetrical diarylamines under mild conditions. However, it has not been tested for sterically demanding aryl boronic acids and aryl nitroso compounds. The reaction was performed in DMF, as previously described.[15] Two combinations of the reactants were tested: *ortho*-*tert*-butylnitrosobenzene with *para*-*tert*-butylphenyl boronic acid and the opposite combination. The first reaction was very efficient, leading to unsymmetrical 2,4′-bis(*tert*-butylphenyl)amine in a practical yield (81%), contrary to oxidative amination (see above). Thus, we can conclude that, for synthesis of bulky *ortho*-substituted diarylamines, reductive amination of aryl boronic acid is more rational, compared with oxidative amination. However, the reaction was relatively slow and, to obtain better yield, prolonged heating was required (16 h at 60 °C). The opposite combination of reactants with the bulky *tert*-butyl group in the *ortho* position of the phenyl boronic acid resulted in the same unsymmetrical diarylamime in much lower yield (56%) by using the same reaction protocol.

The significantly lower yield of 2,4′-bis(*tert*-butylphenyl)amine obtained in the latter case indicates that the aryl boronic acid is more sterically demanding in both oxidative and reductive amination, compared with the N-containing component. This can be explained by greater bulkiness of the $B(OH)_2$ fragment compared with amino and nitroso groups. According to the results of DFT calculations, the conjugation of the boron atom with the phenyl ring in the *ortho*-*tert*-butylphenyl boronic acid is almost completely disturbed; the torsion O–B–C–C angle is about 66° due to repulsion between *tert*-butyl and $B(OH)_2$ moieties. The reaction can be expected to proceed via a tetracoordinated intermediate or transition state (see below); both are extremely unfavorable because the addition of the fourth addend at the boron atom will additionally increase steric repulsion between the *tert*-butyl group and the boron-containing fragment.

This allows us to conclude that insertion of bulky substituents into the *ortho* position of aryl boronic acids dramatically decreases their activity in reductive and, especially, oxidative amination.

To estimate the steric penalty that we had to overcome, computations on the geometries and electronic structures of the isomeric bulky amines were performed. Results revealed a significant energy difference between 4,4′-bis(*tert*-butylphenyl)-amine and 2,4′- and 2,2′-isomers: the relative free energies of the isomers were 0, 4.8, and 9.9 kcal mol^{-1}, respectively. A significant decrease in the thermodynamic stability across the series indicates increasing repulsive interactions within the molecules.

Evidently, the most difficult case was to obtain 2,2′-bis(*tert*-butylphenyl)amine. The experimental data discussed above clearly indicate that the application of reductive amination gives a better chance of reaction. The reaction was performed according to the same procedure as that described above for unsymmetrical 2,4′-bis(*tert*-butylphenyl)amine. However, the temperature was increased up to 150 °C because a drastic decrease in the reaction rate could be expected due to a significant increase in steric demands. After 9 h of heating and a standard workup procedure, the target 2,2′-bis(*tert*-butyl)amine was isolated in 12% yield (along with 28% of the starting *ortho*-*tert*-butylnitrosobenzene). Additionally, some *tert*-butylbenzene was detected in the reaction mixture. This is in agreement with data reported in the literature,[25] which indicates that typical competing paths, in this case, are protodeboronation and homocoupling. Such a low yield of 2,2′-bis(*tert*-butylphenyl)amine, despite prolonged heating at high temperature, indicates that the combination of two *ortho*-substituted reactants is extremely unfavorable.

HRMS data confirmed that the reaction product was the target amine; the signal of the molecular ion and a characteristic isotopic distribution were observed. However, the steric bulkiness of the isomer resulted in some special features of the spectrum compared with that of 2,4′-bis(*tert*-butylphenyl) amine (see below for the details).

The data obtained are summarized in Table 1.

Because the results obtained for isomeric bis(*tert*-butylphenyl)amines provide evidence that reductive amination is preferable for the synthesis of bulky diarylamines, this approach was used to obtain a series of new trifluoromethylated diarylamines. The reaction procedure was similar to that described above. The *ortho*-/*para*-trifluoromethylated phenyl boronic acids were synthesized as described in the literature.[24] As the nitroso component, *ortho*-/*para*-*tert*-butyl- and trifluoromethyl-substituted nitrosobenzenes were used. The results obtained are given in Table 2. All trifluoromethyl-containing diphenylamines were obtained as fusible white crystals that were soluble in hydrocarbons (hexane, toluene).

Interestingly, the yields for CF_3-substututed diarylamines were lower than those for the amines containing only *t*Bu groups, although the latter were more bulky (see Table 1). As

Table 1. Yields of isomeric bis(*tert*-butylphenyl)amines in oxidative ($Cu(OAc)_2$ (1.5 equiv), Et_3N (2.5 equiv), 25 °C, CH_2Cl_2, O_2) and reductive amination (CuCl (1 equiv), DMF, Ar, 60 °C).

	Oxidative amination			Reductive amination		
	*t*Bu-$C_6H_4NH_2$	*t*Bu-C_6H_4-$B(OH)_2$	Yield [%]	*t*Bu-C_6H_4NO	*t*Bu-C_6H_4-$B(OH)_2$	Yield [%]
4,4′-	*para*-	*para*-	65	*para*-	*para*-	82
2,4′-	*ortho*-	*para*-	22	*ortho*-	*para*-	81
2,4′-	*para*-	*ortho*-	7	*para*-	*ortho*-	56
2,2′-				*ortho*-	*ortho*-	12

Table 2. Reductive amination of aryl boronic acids with substituted nitrosobenzenes (CuCl (1 equiv), DMF, Ar, 60 °C).

	x-C_6H_4NO	*y*-$C_6H_4B(OH)_2$	Yield [%]
1	4-CF_3	2-CF_3	41
2	4-*t*Bu	4-CF_3	50
3	4-*t*Bu	2-CF_3	traces
4	2-CF_3	4-*t*Bu	70
5	2-*t*Bu	4-CF_3	41

shown above, *ortho*-substituted aryl boronic acids are less reactive. This is the reason for the better yields obtained when *para*-substituted boronic acids are used (compare Table 2, entries 2 and 3). However, how can the dramatic difference in yields obtained in the reaction of 2-CF_3-$C_6H_4B(OH)_2$ with *para*-*t*Bu- and CF_3-substituted nitrosobenzenes (Table 2, entries 1 and 3) be explained? It is probable that the electronic properties of the substituents also play a role. DFT calculations to determine the reaction mechanism clarified the situation (see below).

Spectral characterization of amines

^1H, ^{13}C, and ^{19}F NMR spectral characterization of new amines, with complete assignment of signals, was performed in $CDCl_3$ (see the Supporting Information). For 2,2′-bis(*tert*-butylphenyl) amine, the assignment of the signals in the ^1H NMR spectra was based on the double-resonance experiment. For assignment of the signals in ^1H and ^{13}C NMR spectra for the other amines, 2D NMR spectroscopy techniques (HMBC and HSQC) were applied.

The ESI-HRMS data for all amines showed the signal corresponding to the molecular ion; the isotopic distribution observed in the spectra coincided with theoretical values (see the Supporting Information). Notably, for 2,2′-bis(*tert*-butylphenyl)-amine, the $[M+H]^+$ signal appeared in the ESI-MS spectrum only after a small excess of formic acid was added to the sample. Thus, protonation of this compound under ESI conditions is impeded. Evidently, the lone pair of the nitrogen atom is shielded by two bulky *ortho*-*tert*-butyl groups. Less basic 2,4′-bis(trifluoromethylphenyl)amine is also difficult to protonate, but it is prone to lose a proton, yielding anions that can be detected in the mass spectrum recorded in negative mode.

A comparative analysis of the IR data for the isomeric bis(-*tert*-butylphenyl)amines was performed. The IR spectrum of 2,4′-bis(*tert*-butylphenyl)amine exhibits a characteristic absorption at the following frequencies, confirming its structure (the corresponding values for 4,4′-bis(*tert*-butylphenyl)amine taken from ref. [26] are given in parentheses for comparison): $\tilde{\nu}=$ 3445 (3374), N–H; 3023, 3047, 3083, 3100 (3055, 3031), C–H_{Ar}; 2866, 2901, 2957 (2903, 2863, 2963), $C(CH_3)_3$; 1571, 1581, 1595, 1612 (1571, 1581, 1595, 1612), C=C_{Ar}; 1514 cm^{-1} (1477), C–$N_{Ar\text{-}N\text{-}Ar}$. The most informative result is a comparison of the vibrations related to the amino group. Significantly higher frequency values of the N–H and C–N bonds observed for the 2,4′-isomer might be attributed to the influence of the neighboring bulky group. It should be mentioned that for all amines investigated herein the ν(N–H) values for the *ortho*-*para*-substituted derivatives are higher than those of di-*para*- isomers (e.g., compare: $\tilde{\nu}=3400$ (for 4-*t*Bu, 4′-CF_3), 3433 (for 2-*t*Bu, 4′-CF_3), and 3458 cm^{-1} (for 4-*t*Bu, 2′-CF_3)). The N–H stretching band is much more intensive for trifluoromethylated derivatives (the maximal intensity was observed for 2.4′-bis(trifluoromethylphenyl)amine), which indicated enhanced N–H bond polarity.

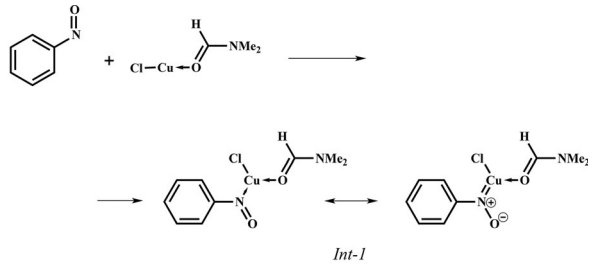
Reductive amination: DFT mechanistic study

Some mechanistic considerations of oxidative N-arylation were described in an earlier report.[18] They were based on the analysis of byproducts, base and solvent effects, as well as an empirical study of the influence of substrate electronic properties. The results obtained shed some light on the N–C cross-coupling reaction, but were not supported by a theoretical (e.g., DFT) study. For reductive copper-mediated N-arylation, only the general scheme of the reaction steps was proposed,[15] but was not supported with any computational data or experimental observations of the reaction intermediates.

Herein, DFT elucidation of the mechanism of reductive arylation of nitroso arenes with aryl boronic acids was performed. The relative energies of possible intermediates and activation barriers for the each step were determined.

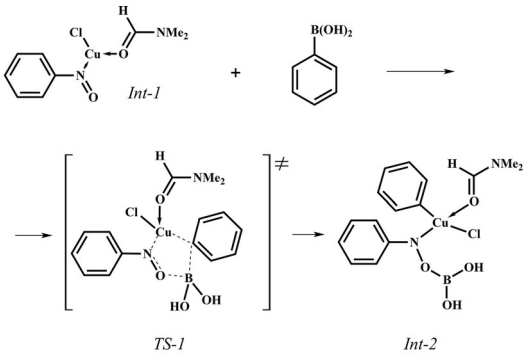
As follows from the results obtained, the first step (Scheme 3) is barrierless and the formation of *Int-1* is exothermic ($\Delta E_0=-20.3$ kcal mol^{-1}; $\Delta G^0_{298}=-9.5$ kcal mol^{-1}; $\Delta E^{\neq}_0=$ 0 kcal mol^{-1}).

It is followed by a transmetalation-type phenyl-transfer step, which is slightly endothermic ($\Delta E_0=+0.7$ kcal mol^{-1}), but the Gibbs free energy, $\Delta G^0_{298}=+13.5$ kcal mol^{-1}, is significantly more positive due to a decrease in entropy (Scheme 4). The reaction proceeds via the five-membered cyclic transition state, which corresponds to a relatively high barrier of 24.0 kcal mol^{-1}. It should be mentioned that transmetalation is usually



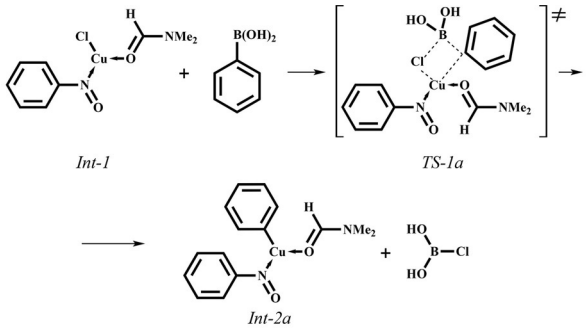
ΔE_0 = -20.3 kcal mol^{-1}; ΔG^0_{298} = -9.5 kcal mol^{-1}; $\Delta E_0^{\ddagger}$ = 0 kcal mol^{-1}

Scheme 3. Activation of the nitroso component with copper(I) (energies were calculated at the PBE/Λ22 level).



ΔE_0 = 0.7 kcal mol^{-1}; ΔG^0_{298} = 13.5 kcal mol^{-1}; $\Delta E_0^{\ddagger}$ = 24.0 kcal mol^{-1}

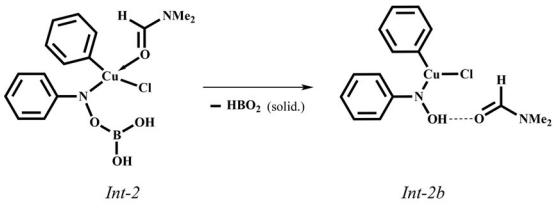
Scheme 4. Transmetalation-type transformation (energies were calculated at the PBE/Λ22 level).



ΔE_0 = 23.4 kcal mol^{-1}; ΔG^0_{298} = 23.4 kcal mol^{-1}; $\Delta E_0^{\ddagger}$ = 29.2 kcal mol^{-1}

$$\mathbf{Cl\text{-}B(OH)_2\ (gas)} \longrightarrow \mathbf{HBO_2\ (solid) + HCl\ (gas)}$$

ΔH^0_{298} = -22.7 kcal mol^{-1}; ΔG^0_{298} = -17.4 kcal mol^{-1}



ΔG^0_{298} = -23.1 kcal mol^{-1}

Scheme 5. An alternative route (energies were calculated at the PBE/Λ22 level).

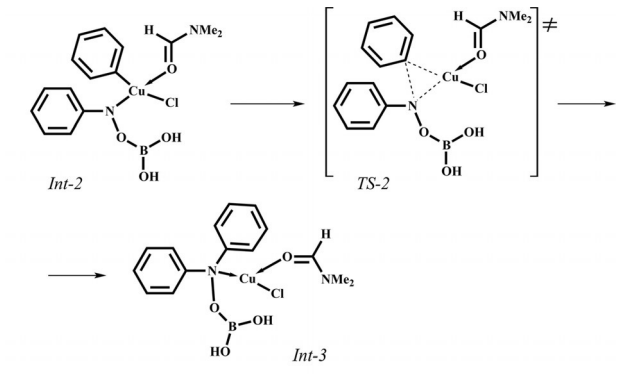
considered to be a rate-determining step for reactions of this type.[27] An alternative mechanism for the transmetalation-type step can be also suggested (Scheme 5). It is based on the less favorable four-membered transition state with a higher activation barrier ($\Delta E_0^{\ddagger}$ = 29.2 kcal mol^{-1}) and is significantly endothermic (ΔE_0 = 23.4 kcal mol^{-1}, ΔG^0_{298} = 23.4 kcal mol^{-1}). This is attributed to the lower energy of the B–Cl bond, compared with that of B–O, which is formed in the previous case. Thermodynamically unfavorable *Int-2* can be easily stabilized through the elimination of metaboric acid; the latter can be also formed after $ClB(OH)_2$ decomposition.

Thermodynamic parameters of these reactions were estimated by applying the Hess principle. To simplify calculations and minimize inaccuracy, thermodynamic parameters from the NIST Chemistry Webbook database[28] for gaseous $B(OH)_3$, H_2O, and solid HBO_2 were used, as well as the calculated parameters for gaseous H_2O, $ClB(OH)_2$, $B(OH)_3$, and HCl. Application of this procedure gives the following estimation for the Gibbs free energy values for two transmetalation routes given above, yielding *Int-2b* and *Int-2a*: $\Delta G^0_{298} = -9.6$ kcal mol^{-1} and $\Delta G^0_{298} = +6$ kcal mol^{-1}, respectively.

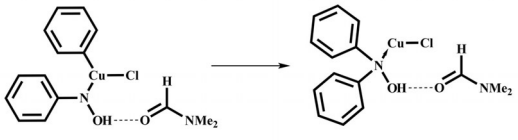
The steric penalty due to the presence of the *ortho-tert*-butyl group either in the nitroso component or in the boronic acid was examined for the transmetalation step. It appears that the reaction barrier for the bulky nitroso compound is almost the same as that for the unsubstituted one. Meanwhile, the introduction of the *o*-*t*Bu group in the aryl boronic acid molecule leads to a significant increase in the activation energy ($\Delta E_0^{\ddagger}$ = 32.1 kcal mol^{-1} versus 24.0 kcal mol^{-1} for phenyl boronic acid). This result is in line with our experimental observations on much lower yields of the product when hindered boronic acids are used for the coupling.

The influence of the donor (*t*Bu) and acceptor (CF_3) substituents in the boron or nitroso components on this reaction step was investigated. Four combinations of reactants were considered: the electron-poor nitroso compound (4-CF_3-nitrosobenzene) with electron-rich boronic acid (4-*t*Bu-phenyl boronic acid) and vice versa (4-*t*Bu-nitrosobenzene with 4-CF_3-phenyl boronic acid), as well as two combinations with the same substituents in the reactants. The computational results obtained revealed almost no difference between these combinations: the activation energy was about 23 kcal mol^{-1} in all cases (4-*t*BuC_6H_4 $B(OH)_2$/4-$CF_3C_6H_4NO$: 23.1 kcal mol^{-1}; 4-$CF_3C_6H_4B(OH)_2$/4-*t*BuC_6H_4NO: 22.9 kcal mol^{-1}; 4-*t*Bu$C_6H_4B(OH)_2$/4-*t*BuC_6H_4NO: 23.7 kcal mol^{-1}; 4-$CF_3C_6H_4B(OH)_2$/4-$CF_3C_6H_4NO$: 23.2 kcal mol^{-1}) similar to that for the unsubstituted compounds. This testifies in favor of a concerted process with the cyclic rearrangement of the bonds.

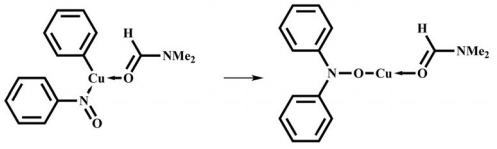
Intermediates *Int-2*, *Int-2a*, and *Int-2b* formed in the transmetalation steps are prone to reductive elimination, yielding the C–N–C framework and are converted into structurally similar intermediates (*Int-3*, *Int-3a*, *Int-3b*). Transformations of *Int-2* and *Int-2b* intermediates have relatively low activation barriers and are thermodynamically favorable, whereas a similar process for



ΔE_0 = -21.8 kcal mol^{-1}; ΔG^0_{298} = -20.8 kcal mol^{-1}; $\Delta E_0^{\ddagger}$ = 3.5 kcal mol^{-1}

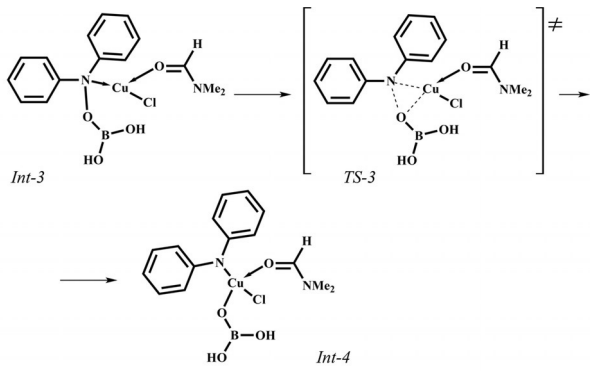


ΔE_0 = -18.7 kcal mol^{-1}; ΔG^0_{298} = -18.3 kcal mol^{-1}; $\Delta E_0^{\ddagger}$ = 6.0 kcal mol^{-1}

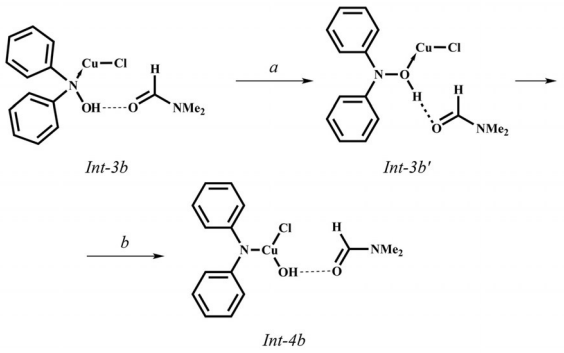


ΔE_0 = -14.9 kcal mol^{-1}; ΔG^0_{298} = -12.5 kcal mol^{-1}; $\Delta E_0^{\ddagger}$ = 20.8 kcal mol^{-1}

Scheme 6. Three possibilities for reductive elimination step and corresponding thermodynamic and kinetic parameters (PBE/Λ22).



ΔE_0 = -11.9 kcal mol^{-1}; ΔG^0_{298} = -12.6 kcal mol^{-1}; $\Delta E_0^{\ddagger}$ = 13.4 kcal mol^{-1}



$\Delta E_{0,a}$ = 4.1 kcal mol^{-1}; $\Delta G^0_{298,a}$ = 3.6 kcal mol^{-1}; $\Delta E_{0,a}^{\ddagger}$ = 10.4 kcal mol^{-1}

$\Delta E_{0,b}$ = -6.8 kcal mol^{-1}; $\Delta G^0_{298,b}$ = -7.6 kcal mol^{-1}; $\Delta E_{0,b}^{\ddagger}$ = 9.5 kcal mol^{-1}

Scheme 7. Oxidative addition of copper(I) to the N–O bond and corresponding thermodynamic and kinetic parameters (PBE/Λ22).

Int-2a requires high activation energy and has a smaller thermodynamic driving force (Scheme 6):

Following on from the reactions given above, the formation of the Ar–N–Ar" moiety proceeds through transmetalation and reductive elimination steps; in subsequent intermediates (Scheme 7, bottom), it is not altered. Hence, the electronic effects of the substituents are more likely appear only in these two reaction steps. As shown above, the transmetalation-type step is "electronically insensitive". Thus, if the reaction is influenced by the electronic nature of the substituents in the reactants, it is the reductive elimination step that should be sensitive to the electronic effects. The electronic influence of the substituents in the *para* position of both reactants on the activation energy of the reductive elimination step was studied. The calculation revealed that the electron-donating *t*Bu group in the aryl boronic acid and the electron-withdrawing CF_3 group in the nitroso compound decreased the activation barriers (relative to the unsubstituted reactants), whereas the opposite combination led to higher barriers (Table 3). As a result, the activation barrier for the latter case is 1.5 times higher than that in the former combination. These computational results are in agreement with experimental data.

A higher activation barrier of this step results in a larger lifetime of the Ar–Cu intermediates (*Int-2* and *Int-2b*). Because these species are expected to be rather reactive, a high activation energy for the reductive elimination should result in an increasing impact of side reactions (e.g., Cu–C bond homolysis or protonation). These results are in accordance with our experimental findings. Thus, the yield of the asymmetric *tert*-butylphenyltrifluoromethylphenyl amine is significantly higher if the electron-donating group is in the aryl boronic acid and the electron-withdrawing group in inserted into the nitroso component (70 and 41%, respectively; Table 2, entries 4 and 5). The unfavorable electronic combination of reactants, coupled with the steric demands of the *ortho*-substituted boronic acid, leads to only traces of the target amine (Table 2, entry 3).

The final step can be considered as oxidative addition of copper(I) to the N–O bond. This step is thermodynamically fa-

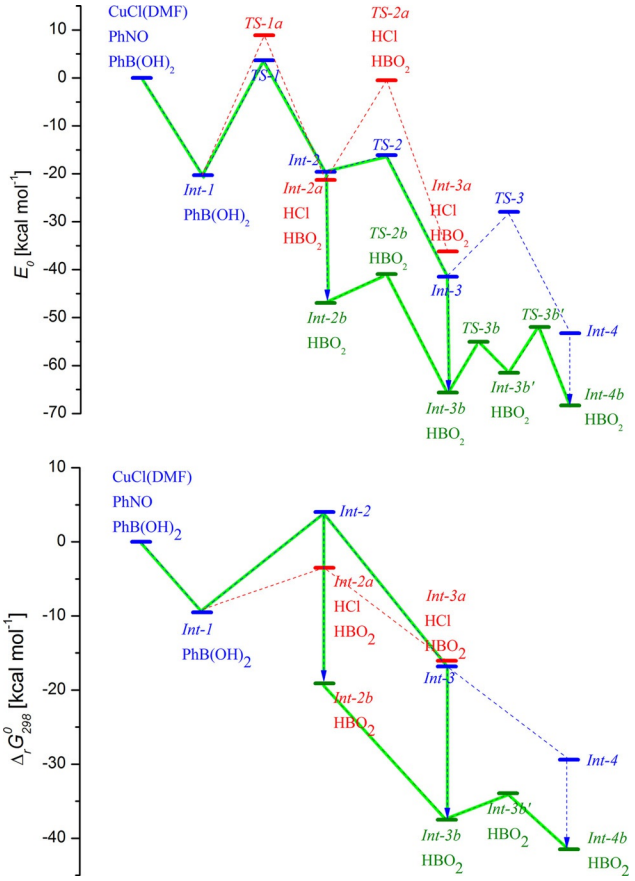
Table 3. Electronic effects of the *para* substituents on the activation barrier for the reductive elimination step.

R group		$\Delta E_0^{\ddagger}$ [kcal mol^{-1}]	
$ArB(OH)_2$	ArNO	*Int-2*→*Int-3*	*Int-2b*→*Int-3b*
H	H	3.5	6.0
*t*Bu	CF_3	2.7	5.1
CF_3	*t*Bu	4.1	7.5
CF_3	CF_3	2.8	6.2
*t*Bu	*t*Bu	3.9	6.3

vorable for both intermediates (*Int-3* and *Int-3b*), but in the latter case a preliminary isomerization step (*Int-3* into *Int-3b*) is required (Scheme 7).

The DFT data described above are summarized in Scheme 8.

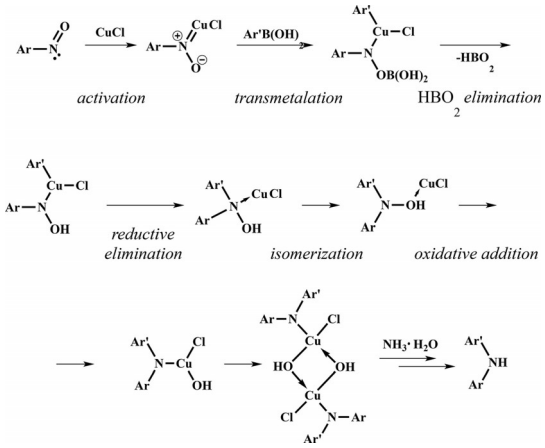
Thus, according to the DFT data, the reaction path consists of four main steps: activation of the nitrosoarene with copper(I); transmetalation, yielding the copper(II) complex with



Scheme 8. The relative energy (ΔE_0) and Gibbs energy change (ΔG^0_{298}) during the reaction path (PBE/Λ22).

the transfer of the $B(OH)_2$ group to the oxygen atom of the nitroso fragment (more likely, followed by the elimination of HBO_2); reductive elimination, which restores copper(I) species; and oxidative addition of copper(I) to the N–O bond, which produces the copper(III) complex again. The copper(III) complex can be decomposed with NH_3 to yield the target diarylamine. The sequence of steps is summarized in Scheme 9.

As observed in Scheme 9, the copper oxidation state changes as follows: $Cu^{I} \rightarrow Cu^{III} \rightarrow Cu^{I} \rightarrow Cu^{III} \rightarrow Cu^{II}$. This makes the reaction very "visual" because copper complexes have different colors, depending on the oxidation state. Even starting *tert*-butylnitrosobenzenes have different colors (navy blue for the 2-*tert*-butyl-substituted isomer and emerald green for the *para* isomer); the difference is enhanced after CuCl addition to the nitroso compound, yielding violet (in the case of 4-*tert*-butylnitrosobenzene) or light green (for 2-*tert*-butylnitrosobenzene) solutions. Subsequent heating with boronic acid results



Scheme 9. Overall reaction scheme of the process described herein.

in a gradual change of the solution color to yellow (corresponding, probably, to copper(I) intermediates *Int-3b* and *Int-3b′*) and then to dark brown (inherent of the final copper(III) complex). A UV/Vis spectroscopy investigation of the reaction mixture was performed. The absorption at $\lambda = 464$ nm was detected; a similar absorbance ($\lambda = 444$ nm) was assigned to the $Cu^{III}_2O_2$ dimeric complex,[29] which resembled the dimeric structure given in Scheme 9. The small difference in the wavelength value can be attributed to the difference in the ligand structure. DFT calculations revealed that dimerization of *Int-4b* to form a binuclear copper species is favorable ($\Delta G^0_{298} = -19$ kcal mol^{-1}), which suggests that this complex likely to be the reaction product. Treatment of the final complex with aqueous ammonia yields the target diarylamine and blue solution of the copper(II) tetraamine complex (through ligand exchange and intramolecular oxidation of the coordinated ammonia).

It is worth mentioning that a certain amount of 4,4′-di-*tert*-butylbiphenyl was isolated as a byproduct in the reaction of 2-*tert*-butylnitrosobenzene with 4-*tert*-butylphenylboronic acid. Similarly, a certain amount of 4,4′-di(trifluoromethyl)biphenyl was obtained in the reaction of 2-*tert*-butylnitrosobenzene with 4-trifluoromethylphenyl boronic acid. These experimental facts confirm the formation of the copper(III) intermediate (*Int-2*, *Int-2b*). It is known that $ArCu^{III}$ complexes are prone to C–Cu bond homolysis, yielding aryl radicals that are easily dimerized. The impact of this side process is not too significant because reductive elimination, resulting in C–N coupling, has a low activation barrier (3.5 and 6.0 kcal mol^{-1} for *Int-2* and *Int-2b*, respectively) and is thermodynamically favorable. However, an electronically or sterically unfavorable combination of the substituents in the reactants (see above) facilitates side processes. Copper(III) intermediates have been also postulated previously.[15]

Conclusion

It was demonstrated that oxidative and reductive copper-assisted amination of aryl boronic acids with arylamines or nitroso benzenes, respectively, which did not require the use of precious metals, expensive ligands, or reactive organometallic

reagents, constituted a practical method for the synthesis of a new series of bulky diarylamines with *ortho*-/*para*-*tert*-butyl and trifluoromethyl substituents in the aromatic rings. A comparative investigation of the oxidative and reductive approaches indicated that, to obtain sterically demanding diarylamines, reductive amination is preferable. The steric bulkiness of the new *ortho*-substituted bis(*tert*-butylphenyl)amines that impeded the synthetic procedure was estimated; relative free energies of the 4,4′-, 2,4′-, and 2,2′ isomers were 0, 5.3, and 11.0 kcal mol^{-1}, respectively. A significant decrease in the thermodynamic stability in the series indicates increasing repulsive interactions within the molecules. For previously known bis(isopropylphenyl)amines,[30] the free energy difference for 4,4′ and 2,2′ isomers is substantially lower (only 3.9 kcal mol^{-1}).

To obtain a better yield of the unsymmetrical diarylamine, a bulky substituent should be located in the N-containing component (the nitroso compound), rather than in the corresponding aryl boronic acid. DFT estimation of the mechanism of copper(I)-assisted reductive amination of boronic acids with aryl nitroso compounds was performed, possible active species were identified, and a detailed potential-energy profile for feasible reaction paths was calculated.

DFT estimation of the steric penalty revealed that the reaction barrier for the transmetalation step for the hindered nitroso compound was almost the same as that for the unsubstituted one, whereas the introduction of the *o*-*t*Bu group in the boronic acid molecule led to a significant increase in the activation energy ($\Delta E_0^{\neq} = 32.1$ kcal mol^{-1} versus 24.0 kcal mol^{-1} for phenyl boronic acid).

DFT estimations showed that electronic effects of the substituents were most significant in the reductive elimination step. Calculations revealed that the optimal combination for the synthesis of asymmetric diarylamines was the insertion of the electron-donating substituent into the aryl boronic acid and the electron-withdrawing group in the nitroso compound. This decreased the activation barriers (relative to the unsubstituted reactants) and provided better yields, whereas the opposite combination led to higher barriers and lower yields of diarylamines.

By using the aforementioned guidelines, a series of new diarylamines containing bulky *tert*-butyl- and trifluoromethyl substituents in different positions of the aromatic rings was obtained and fully characterized by HRMS and NMR and IR spectroscopy methods. These bulky *ortho*-substituted diarylamines are of interest as precursors for the corresponding stable nitroxides, which are prospective structurally tunable redox-active materials.

We hope that the guidelines given above will be helpful for choosing an optimal synthetic procedure, leading to unsymmetrical bulky diarylamines.

Experimental Section

General information

Mass spectra were measured with a high-resolution time-of-flight instrument by using electrospray ionization (ESI-MS).[20] Measurements were performed in positive-ion mode, with an interface capillary voltage of 4.5 kV, an effective scan range of *m/z* 100–1200, external calibration (0.016 M sodium formate in a 1:1 mixture of CH_3CN/water or ESI-L low-concentration tuning mix, Agilent Technologies), direct syringe injection at a flow rate of 3 μL min^{-1}, nitrogen as the dry gas at 4 L min^{-1}, and an interface temperature of 180 °C. ^{1}H (400.0 MHz) and ^{13}C NMR (100.6 MHz) spectra were recorded in $CDCl_3$. Chemical shifts were referenced to a residual nondeuterated solvent. ^{19}F NMR chemical shifts were referenced to $CFCl_3$.

Computational details

DFT calculations for the reductive amination mechanism were performed in the PRIRODA quantum chemistry program.[31,32] The gradient-corrected exchange-correlation Perdew, Burke, and Ernzerhof (PBE) functional,[33] and double-zeta quality basis set Λ01 were used for preliminary searches of the intermediates and transition states. Triple-zeta quality basis set Λ22, along with the PBE functional, was used for structure optimizations and thermal correction calculations.[34] The 10^{-6} threshold on the molecular gradient at the geometry optimization procedure was employed.

Oxidative amination (Chan–Lam coupling) of 4,4′-bis(*tert*-butylphenyl)amine

Anhydrous copper(II) acetate (2.15 g, 11.8 mmol) was added to a stirred solution of *para*-*tert*-butylaniline (880 mg, 5.9 mmol), *para*-*tert*-butylphenyl boronic acid (1.58 g, 8.9 mmol), and triethylamine (2.5 mL, 18 mmol) in CH_2Cl_2 (20 mL). The slurry was stirred under ambient conditions for 48 h and filtered; the filtrate was evaporated and the residue was purified by column chromatography on silica gel (toluene/hexane 1:9) to give 4,4′-bis(*tert*-butylphenyl)amine as white crystals (1.08 g, 65%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta =$ 7.32–7.27 (m, 4H), 7.05–6.99 (m, 4H), 5.59 (s, 1H), 1.32 ppm (s, 18H); IR (ATR, ZnSe): $\tilde{\nu} =$ 3375, 3051, 3032, 2954, 2900, 2862, 1606, 1514, 1475, 1462, 1390, 1360, 1346, 1311, 1265, 1242, 1188, 1163, 1111, 1011, 822, 548 cm^{-1}.

2,4′-Bis(*tert*-butylphenyl)amine

Unsymmetrical 2,4′-bis(*tert*-butylphenyl)amine was obtained as white crystals (22%) by using the same protocol. M.p. 86–88 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.40$ (dd, $^3J = 7.9$, $^4J = 1.5$ Hz, 1H; *o*-Ph), 7.28 (dd, $^3J = 7.9$, $^4J = 1.5$ Hz, 1H; *o*-Ph), 7.25–7.21 (m, 2H; *p*-Ph), 7.14 (ddd, $^3J = 7.9$, 7.3, $^4J = 1.6$ Hz, 1H; *o*-Ph), 7.01 (ddd, $^3J = 7.9$, 7.3, $^4J = 1.5$ Hz, 1H; *o*-Ph), 6.83–6.79 (m, 2H; *p*-Ph), 5.37 (s, 1H; 7-H_N), 1.45 (s, 9H; 15-H_{tBu}), 1.31 ppm (s, 9H; 1-H_{tBu}); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 143.0$ (*p*-Ph), 142.6 (*o*-Ph), 142.19 (*o*-Ph), 142.05 (*p*-Ph), 127.0 ($CH_{o\text{-}Ph}$), 126.93 ($CH_{o\text{-}Ph}$), 126.18 ($CH_{p\text{-}Ph}$), 124.47 ($CH_{o\text{-}Ph}$), 123.07 ($CH_{o\text{-}Ph}$), 116.65 ($CH_{p\text{-}Ph}$), 34.90 (*t*Bu), 34.19 (*t*Bu), 31.68 (Me*t*Bu), 30.70 ppm (Me*t*Bu); ESI-HRMS: *m/z* calcd for $C_{20}H_{28}N$ [M+H$^+$]: 282.2216; found: 282.2217; IR (ATR, ZnSe): $\tilde{\nu} =$ 3445, *N-H*; 3023, 3047, 3083, 3100, C–H_{Ar}; 2866, 2901, 2957, C(CH_3)$_3$; 1571, 1581, 1595, 1612, C=C $_{Ar}$; 1514 cm^{-1}, C–$N_{Ar\text{-}N\text{-}Ar}$.

General procedure for reductive amination

Synthesis was performed under an argon atmosphere by using standard Schlenk techniques. A solution of nitrosoarene (0.80 mmol) in dry deaerated DMF (20 mL) was added to an argon-filled two-necked flask, containing CuCl (79 mg, 0.80 mmol), fitted with a reflux condenser and pressure-equalizing dropping funnel. The mixture was stirred at 60 °C (water bath) for 30 min. Then a solution of aryl boronic acid (0.87 mmol) in dry deaerated DMF

(7 mL) was added and the mixture was stirred for 16 h at 60 °C. The color of the solution changed from light green to black via light yellow, green, and greenish blue. Afterwards, the mixture was diluted with water (100 mL), rinsed with a saturated aqueous solution of ammonia (50 mL), and extracted with diethyl ether. Diethyl ether fractions were dried with anhydrous sodium sulfate, solvent was evaporated, and the product was purified by column chromatography on silica gel.

2,4′-Bis(*tert*-butylphenyl)amine: 2,4′-Bis(*tert*-butylphenyl)amine was obtained in 81% yield by using the standard protocol from 2-*tert*-butylnitrosobenzene and 4(*tert*-butyl)phenyl boronic acid. A 1:20 mixture of toluene/hexane was used as an eluent for the purification of the title compound by column chromatography.

4-(Trifluoromethyl)-4′-*tert*-butyldiphenylamine: 4-(Trifluoromethyl)-4′-*tert*-butyldiphenylamine was obtained in 50% yield by using the standard protocol from 4-*tert*-butylnitrosobenzene and 4-(trifluoromethyl)phenyl boronic acid. A mixture of toluene/hexane (1:4) was used as an eluent for the purification of the title compound by column chromatography. ^{1}H NMR: $\delta = 7.48$–7.44 (m, 2H; *o*- vs. CF_3), 7.03–6.99 (m, 2H; *m*- vs. CF_3), 7.39–7.35 (m, 2H; *o*- vs. *t*Bu), 7.13–7.09 (m, 2H; *m*- vs. *t*Bu), 5.89 (s, 1H; NH), 1.35 ppm (s, 9H; *t*Bu); ^{13}C NMR: $\delta = 147.4$ (*p*- vs. CF_3), 146.4 (*ipso*(*t*Bu)), 138.5 (*p*- vs. *t*Bu), 126.8 (q, ^3J(C,F) = 3.8 Hz; *o*- vs. CF_3), 124.9 (q, ^1J(C,F) = 289.8 Hz; CF_3), 121.3 (q, ^2J(C,F) = 32.8 Hz; *ipso*(CF_3)), 126.5 (*o*- vs. *t*Bu), 120.4 (*m*- vs. *t*Bu), 114.9 (*o*- vs. CF_3), 34.5 (quat. *t*Bu), 31.6 ppm (*t*Bu); ^{19}F NMR: $\delta = -61.4$ ppm (CF_3); ESI-HRMS: *m/z* calcd for $C_{17}H_{19}F_3N$ $[M+H]^+$: 294.1464; found: 294.1466; IR (ATR, ZnSe): $\tilde{\nu}$ = 3400, 2964, 2904, 2870, 1608, 1527, 1518, 1396, 1327, 1186, 1161, 1113, 1066, 1011, 825 cm^{-1}.

2-(Trifluoromethyl)-4′-*tert*-butyldiphenylamine: 2-(Trifluoromethyl)-4′-*tert*-butyldiphenylamine was obtained in 70% yield by using the standard protocol from 2-(trifluoromethyl)nitrosobenzene and 4-*tert*-butylphenyl boronic acid. A mixture of toluene/hexane (1:8) was used as an eluent for the purification of the title compound by column chromatography. ^{1}H NMR: $\delta = 7.55$ (d, $^3J = 7.8$ Hz, 1H; *o*- vs. CF_3, *m*- vs. NH), 7.38–7.27 (m, 4H; *m*- vs. CF_3, *o*- vs. NH, *p*- vs. CF_3, *m*- vs. NH, *o*- vs. *t*Bu), 7.11–7.06 (m, 2H; *m*- vs. *t*Bu), 6.90 (t, $^3J = 7.4$ Hz, 1H; *m*- vs. CF_3, *p*- vs. NH), 6.04 (s, 1H; NH), 1.34 ppm (s, 9H; *t*Bu); ^{13}C NMR: $\delta = 146.3$ (*ipso*(*t*Bu)), 142.9 (q, ^3J(C,F) = 1.7 Hz; *o*- vs. CF_3, *ipso*(NH)), 138.8 (*ipso*(NH), *p*- vs. *t*Bu), 132.8 (q, ^5J(C,F) = 1.1 Hz; *p*- vs. CF_3, *m*- vs. NH), 127.0 (q, ^3J(C,F) = 5.4 Hz; *o*- vs. CF_3, *m*- vs. NH), 126.5 (*o*- vs. *t*Bu), 125.0 (q, ^1J(C,F) = 272.4 Hz; CF_3), 120.9 (*m*- vs. *t*Bu), 119.2 (*m*- vs. CF_3, *p*- vs. NH), 117.1 (*m*- vs. CF_3, *o*- vs. NH), 116.7 (q, ^2J(C,F) = 29.3 Hz; *ipso*(CF_3)), 34.5 (quat. *t*Bu), 31.6 ppm (*t*Bu); ^{19}F NMR: $\delta = -61.9$ ppm (CF_3); ESI-HRMS: *m/z* calcd for $C_{17}H_{19}F_3N$ $[M+H]^+$: 294.1464; found: 294.1465; IR (ATR, ZnSe): $\tilde{\nu}$ = 3458, 2966, 2937, 2914, 2868, 1606, 1593, 1520, 1469, 1403, 1363,1327, 1298, 1284, 1244, 1230, 1167, 1107, 1059, 1034, 951, 889, 833, 808, 764, 742, 733, 656 cm^{-1}.

2-*tert*-Butyl-4′-(trifluoromethyl)diphenylamine: 2-*tert*-Butyl-4′-(trifluoromethyl)diphenylamine was obtained in 41% yield by using the standard protocol from 2-*tert*-butylnitrosobenzene and 4-(trifluoromethyl)phenyl boronic acid. A mixture of toluene/hexane (1:8) was used as an eluent for the purification of the title compound by column chromatography. ^{1}H NMR: $\delta = 7.48$ (dd, $^3J = 7.6$, $^4J = 1.8$ Hz, 1H; *o*- vs. *t*Bu, *m*- vs. NH), 7.44–7.39 (m, 2H; *o*- vs. CF_3), 7.27 (dd, $^3J = 7.7$, $^4J = 2.0$ Hz, 1H; *m*- vs. *t*Bu, *o*- vs. NH), 7.23 (td, $^3J = 6.9$, $^4J = 1.7$ Hz, 1H; *p*- vs. *t*Bu, *m*- vs. NH), 7.19 (ddd, $^3J = 7.6$, $^3J = 6.9$, $^4J = 2.1$ Hz, 1H; *m*- vs. *t*Bu, *p*- vs. NH), 6.77–6.72 (m, 2H; *m*- vs. CF_3), 5.79 (s, 1H; NH), 1.42 ppm (s, 9H; *t*Bu); ^{13}C NMR: $\delta = 149.5$ (*p*- vs. *CF*$_3$), 145.7 (*ipso*(*t*Bu)), 139.5 (*ipso*(NH), *o*- vs. *t*Bu), 128.3 (*m*- vs. *t*Bu, *o*- vs. NH), 127.5 (*o*- vs. *t*Bu, *m*- vs. NH), 127.3 (*p*- vs. *t*Bu, *m*- vs. NH), 126.8 (q, ^3J(C,F) = 3.8 Hz; *o*- vs. CF_3), 125.9 (*m*- vs. *t*Bu, *p*- vs. NH), 125.0 (q, ^1J(C,F) = 270 Hz; CF_3), 120.2 (q, ^2J(C,F) = 32.5 Hz; *ipso*(CF_3)), 114.1 (*m*- vs. CF_3), 35.2 (quat. *t*Bu), 30.8 ppm (*t*Bu); ^{19}F NMR: $\delta = -61.2$ ppm (CF_3); ESI-HRMS: *m/z* calcd for $C_{17}H_{19}F_3N$ $[M+H]^+$: 294.1464; found: 294.1465; IR (ATR, ZnSe): $\tilde{\nu}$ = 3433, 3062, 2966, 2877, 1616, 1597, 1572, 1523, 1498, 1481, 1471, 1472, 1442, 1398, 1367, 1325, 1290, 1261, 1240, 1188, 1157, 1128, 1101, 1065, 1007, 945, 877, 829, 764, 742, 729, 694, 652, 631, 607, 588 cm^{-1}.

2,4′-Bis(trifluoromethyl)diphenylamine: 2,4′-Bis(trifluoromethyl)diphenylamine was obtained in 41% yield by using the standard protocol from 2-*tert*-butylnitrosobenzene and 4-(trifluoromethyl)-phenyl boronic acid. Hexane was used as an eluent for the purification of the title compound by column chromatography. ^{1}H NMR: $\delta = 7.64$ (d, $^3J = 8.0$ Hz, 1H), 7.54–7.49 (m, 2H), 7.48–7.44 (m, 2H), 7.14–7.06 (m, 3H), 6.15 ppm (s, 1H); ^{13}C NMR: $\delta = 145.8$, 140.1, 133.0, 127.3 (q, ^3J(C,F) = 5.3 Hz), 126.9 (q, ^3J(C,F) = 3.8 Hz), 124.54 (q, ^1J(C,F) = 271.1 Hz), 124.47 (q, ^1J(C,F) = 273.5 Hz), 123.3 (q, ^2J(C,F) = 33.0 Hz), 122.4, 121.0, 120.5 (q, ^2J(C,F) = 29.5 Hz), 117.3 ppm; ^{19}F NMR: $\delta = -61.60$, -61.75 ppm; ESI-HRMS (negative mode): *m/z* calcd for $C_{14}H_8F_6N$ $[M-H]^+$: 304.0566; found: 304.0566; IR (ATR, ZnSe): $\tilde{\nu}$ = 3452, 2924, 2854, 1608, 1597, 1585, 1527, 1511, 1475, 1462, 1408, 1319, 1288, 1250, 1232, 1186, 1163, 1109, 1093, 1061, 1034, 1009, 953, 881, 841, 762, 737, 665, 652, 596 cm^{-1}.

2,2′-Bis(*tert*-butylphenyl)amine: 2,2′-Bis(*tert*-butylphenyl)amine was obtained in 12% yield by using the same protocol, except the reaction mixture was heated at a higher temperature (150 °C, oil bath). The product was purified by column chromatography on silica gel (with petroleum ether as an eluent). ^{1}H NMR: $\delta = 7.39$ (dd, $^3J = 7.88$ Hz, $^4J = 1.55$ Hz, 1H; *m*- vs. NH, *o*- vs. *t*Bu), 7.08 (ddd, $^3J = 7.29$ Hz, 7.95 Hz, $^4J = 1.55$ Hz, 1H; *m*- vs. NH, *p*- vs. *t*Bu), 6.93 ($^3J = 7.29$ Hz, 7.88 Hz, $^4J = 1.50$ Hz, 1H; *p*- vs. NH, *m*- vs. *t*Bu), 6.91 (dd, 1.39 Hz, 7.95 Hz, 1H; *o*- vs. NH, *m*- vs. *t*Bu), 5.42 (s, 1H; NH), 1.49 ppm (s, 9H; *t*Bu); ^{13}C NMR: $\delta = 144.0$ (*ipso*(NH)), 140.5 (*ipso*(*t*-Bu)), 127.1 (*m*- vs. NH, *p*- vs. *t*Bu), 126.8 (*m*- vs. NH, *o*- vs. *t*Bu), 123.2 (*o*- vs. NH, *m*- vs. *t*Bu), 121.7 (*p*- vs. NH, *m*- vs. *t*Bu), 34.7 (q, *t*Bu), 29.9 ppm (Me); ESI-HRMS: *m/z* calcd for $C_{20}H_{28}N$ $[M+H^+]$: 282.2216; found: 282.2211.

Acknowledgements

This work was supported by the Russian Science Foundation (project number 16-13-10282). NMR spectroscopy parts of this work were supported by the Lomonosov Moscow State University "Program of Development". We would like to acknowledge Thermo Fisher Scientific Inc., MS Analytica (Moscow, Russia), and personally to Prof. Alexander Makarov for providing mass spectrometry equipment for this work.

Conflict of interest

The authors declare no conflict of interest.

Keywords: amination · copper · density functional calculations · reaction mechanisms · steric hindrance

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Manuscript received: May 18, 2017
Accepted manuscript online: July 12, 2017
Version of record online: September 1, 2017