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Apparent Alkyl Transfer and Phenazine Formation via an Aryne Intermediate

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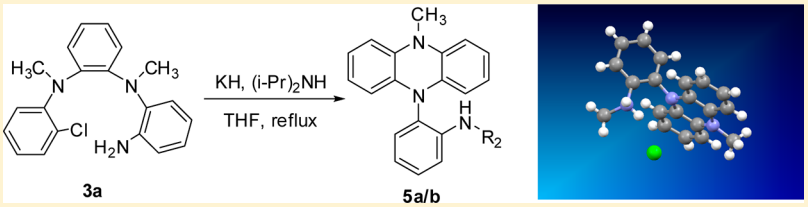
Supporting Information



ABSTRACT: Treatment of chlorotriaryl derivatives **3a** and **3d** or fluorotriaryl derivatives **3b** and **3e** with potassium diisopropylamide afforded alkyl-shifted phenazine derivatives **5a**/**5b**, rather than the expected 9-membered triazaorthocyclophane **2a**. The phenazine derivatives were isolated in 78−98% yield depending on the halogen and alkyl group present. In the absence of the halogen (chloro or fluoro), the apparent alkyl shift proceeds more slowly and cannot proceed via the intermediacy of the aryne intermediate. Mechanistic possibilities include intramolecular nucleophilic attack on an aryne intermediate leading to a zwitterionic intermediate and alkyl transfer via a 5-*endo-tet* process, or via a Smiles rearrangement.

INTRODUCTION

Cyclotriveratrylene (CTV, **1**), a [1.1.1]orthocyclophane, is an archetypal cyclophane scaffold that is commonly employed in supramolecular chemistry.[1−4] As part of our research program directed toward the synthesis and application of apex-modified CTV derivatives[5−7] with unique material properties and applications involving host−guest chemistry,[8] we recently reported the synthesis of the new triazaorthocyclophane **2a**[9] (Figure 1) which was alkylated to give the *N*,*N*′,*N*″-trimethyl

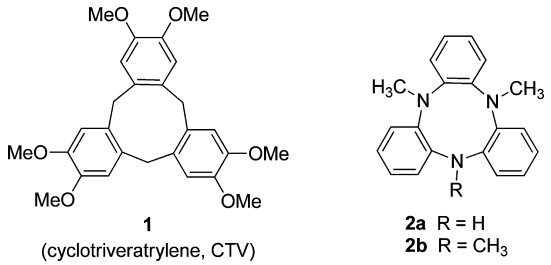
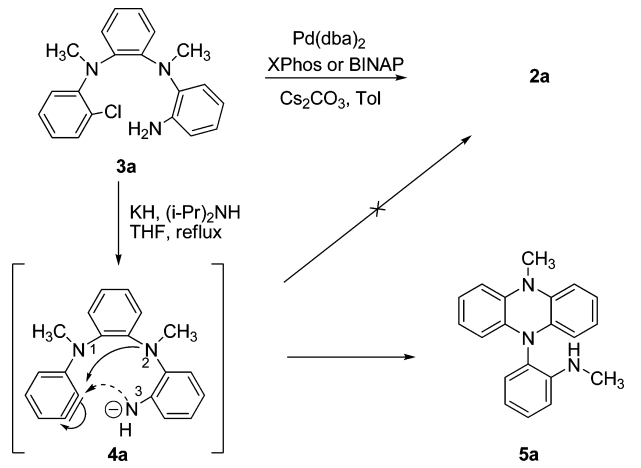


Figure 1. Structures of CTV and 1,4,7-triazacyclononatriene derivatives.

derivative **2b**. Following a six-step linear sequence to obtain the precursor **3a** (Scheme 1), two mechanistically different approaches were examined in order to obtain the final desired triazacyclophane **2a** (Scheme 1). The first method employed a Buchwald−Hartwig N-arylation,[10−13] which was ultimately successful in the macrocyclization of **3a** to azacyclophane **2a**.[9] In parallel, we had also envisioned that the use of benzyne

Scheme 1. Cyclization of 3a via Buchwald−Hartwig Route Yielding Orthocyclophane 2a and Benzyne Route Affording Phenazine 5a



(aryne) intermediate **4a** should be a viable synthetic route to the triazacyclophane skeleton, which led to the observation of an unexpected alkyl transfer and phenazine formation with interesting mechanistic implications that we describe herein.

Ring closures via aryne intermediates were first introduced independently by Bunnett[14] and Huisgen.[15] Since then, aryne

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intermediates have been used extensively in organic synthesis[16] and in the synthesis of natural products.[17] Barluenga et al. exploited the use of benzyne-tethered vinyl or aryllithium compounds to obtain indole and benzo-fused heterocyclic derivatives.[18] The reactivity of aryne intermediates toward nucleophilic attack is attributed to the low energy LUMO, which is a consequence of the "bending" of the triple bond within the ring; decreasing the energy gap between the LUMO of the aryne and the HOMO of the attacking nucleophile enables reaction between the two partners.[19] For generating benzyne intermediates, a well-established method involves treating an aryl halide with a strong base, especially alkali metal aryls/alkyls or amides in ether solvents or liquid ammonia. Limitations arising from these reactions are due to the tendency for the solvent or the base itself to react with the benzyne intermediate, or from reduction of the benzyne via hydride transfer from the α-carbon of an amide base such as lithium diisopropylamide (LDA).[19]

RESULTS AND DISCUSSION

When we treated intermediate **3a** with potassium diisopropylamide (KDA) in THF under reflux in order to form benzyne intermediate **4a**, a curious methyl shift was observed accompanied by the production of an unexpected phenazine derivative **5a** rather than the desired triazaorthocyclophane derivative **2a** (Scheme 1). Reactions that were attempted with lithium diisopropylamide (LDA) were more sluggish and were not as clean. We had expected that the most nucleophilic anilide nitrogen (N^3) would react rather than the neutral, more sterically encumbered, and presumably less nucleophilic tertiary nitrogen (N^2).

Although the high-resolution molecular ion observed at 301.1562 was consistent with the expected molecular formula for orthocyclophane **2a**, the isomeric structure **5a** was suggested by analysis of the spectral data and was ultimately confirmed by single-crystal X-ray analysis of its tosylate and hydrochloride salts (Figure 2 and Figure S1, Supporting Information). Both salts independently afforded X-ray quality crystals from diethyl ether.

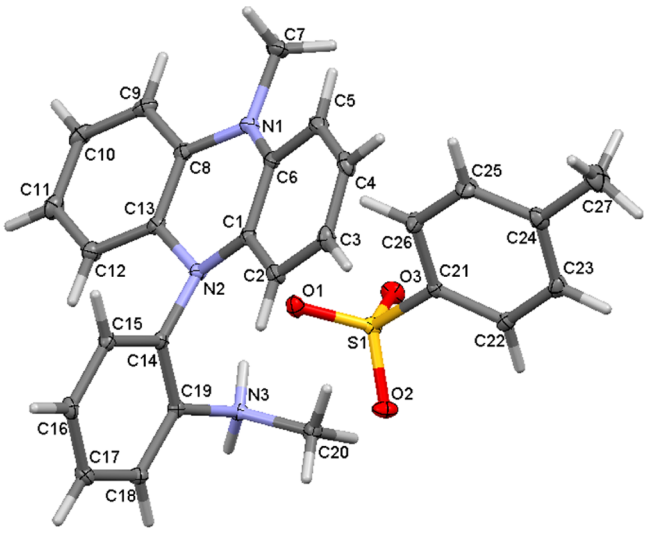

Figure 2. X-ray crystal structure of the methyl-shifted phenazine **5a** as the tosylate salt. Thermal ellipsoid probability level at 50%.

The phenazine byproduct was surprising since molecular models had predicted an ideal overlap of the N^3 anionic anilide lone pair with the in-plane orbital on the proximal alkyne carbon of the benzyne, and we conjectured that the entropic cost of forming the 9-membered ring would not be prohibitive due to the conformational constraints provided by the three intervening aryl rings. Yet 6-membered ring formation with an apparent alkyl shift proceeds exceptionally efficiently, with only the phenazine derivative as the major product formed and isolated (92% yield).

We assumed that intramolecular or intermolecular methyl transfer from N^2 to N^3 was faster than the closure of the 9-membered ring, and might be faster than formation of the benzyne. Thus, we sought to slow down the alkyl transfer. Since S_N2 displacement of a primary center is ~50× slower than of a methyl center,[20] we replaced the N^2-methyl with an *n*-butyl group. Scheme 2 describes the preparation of the requisite *n*-butyl derivative **3d** wherein X = Cl. Adapted from our previous report,[9] intermediate **9a** was alkylated with *n*-butyl bromide to afford *N*-methyl-*N*′-butyl derivative **10d**, which was reduced according to the general method of Sanz[21] to afford **3d**. Ultimately, we also wanted to speed up the formation of the aryne intermediate by utilizing the fluoride substrates (**3b** and **3e**), which commenced via a Buchwald–Hartwig reaction on 2-fluoroiodobenzene (X = F, Y = I) to give the diarylamine **6b** after purification by column chromatography. Methylation of N^1 was accomplished with KOH and Me_2SO_4 in refluxing acetone[22] or with sodium hydride followed by methyl iodide to give 2-fluoro-2′-nitrodiphenylamine **7b**. This was followed by reduction of the nitro group to give aniline **8b** employing the general method of Sanz[21] using CuCl and KBH_4 in dry MeOH. Pd-catalyzed N-arylation of **8b** with *o*-iodonitrobenzene produced the triaryl derivative **9b** in 55% isolated yield after purification. Methylation of N^2 proceeded with KH and MeI in warm DMF, and reduction of the nitro group was once again accomplished using CuCl and KBH_4 to give compounds **10b** and **3b** respectively. Finally, nor-halo substrates **3c** and **3f** (X = H; R = CH_3 or *n*-butyl, respectively) were prepared by Buchwald–Hartwig N-arylation of 2-nitroaniline with bromobenzene to afford **6c**,[23] which was alkylated to give **7c**.[24] Reduction of nitroaniline **7c** gave **8c**, which underwent N-arylation to afford phenylene diamine derivative **9c**. Alkylation with either methyl iodide or *n*-bromobutane gave **10c** and **10f**, respectively, followed by reduction to give **3c** and **3f**, respectively.

As noted above, treatment of starting material **3a** with KDA in THF under reflux afforded phenazine derivative **5a** which had suffered the apparent methyl shift. Table 1 outlines the different reaction conditions and substrates explored. The order in which the alkyl shift is occurring appears to be dependent upon several factors including the halogen leaving group as well as the alkyl group substituent on the internal nitrogen (N^2). When the reaction of chloro-*N*,*N*′-dimethylaniline **3a** was carried out at −78 °C (entry 1) no reaction occurred, as confirmed by 96% recovery of **3a** even though benzyne formation has been observed at this temperature in some cases. However, when the reaction mixture was heated to reflux (66 °C), phenazine **5a** was isolated in 92% yield having suffered the apparent methyl shift (entry 2). In an attempt to slow the rate of an S_N2 reaction, in consideration of the possibility that demethylation *preceded* the formation of the benzyne intermediate and that prior alkyl transfer from N^2 to N^3 was essential for phenazine formation, the incorporation of a more

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Scheme 2. Synthesis of Triaryl Derivatives 3a–f and Formation of Alkyl-Shifted Phenazine Derivatives 5a and 5b

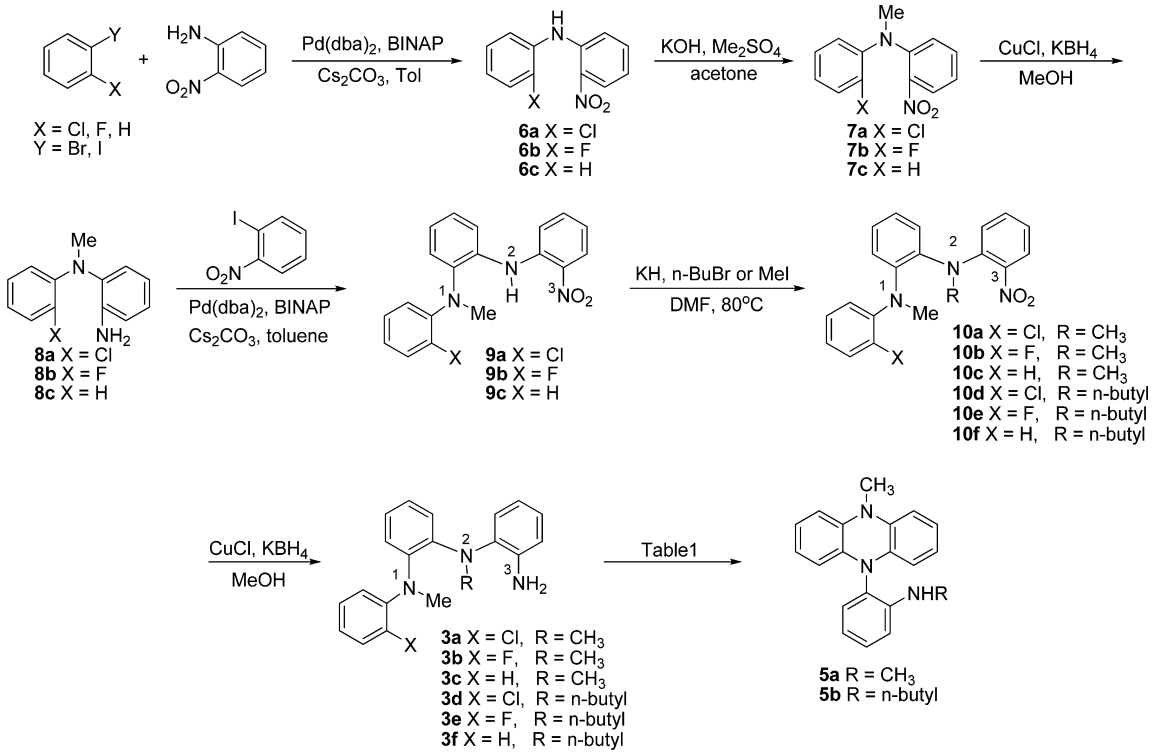
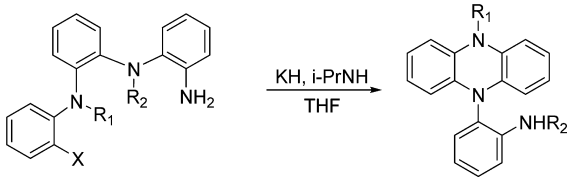


Table 1. Phenazine Formation via Benzyne Intermediates



entry	S.M.	X	R_1	R_2	temp (°C)	product
1	**3a**	Cl	CH_3	CH_3	−78	no reaction
2	**3a**	Cl	CH_3	CH_3	66	**5a**
3	**3b**	F	CH_3	CH_3	66	**5a**
4	**3d**	Cl	CH_3	*n*-butyl	66	no reaction
5	**3d**	Cl	CH_3	*n*-butyl	95	**5b**
6	**3e**	F	CH_3	*n*-butyl	66	**5b**

sterically hindered blocking group was employed. Initial attempts to install an isopropyl substituent led to elimination, though these efforts were not exhaustive, so an *n*-butyl group on the internal nitrogen (N^2) was employed since S_N2 displacement of a primary center is ∼50× slower than of a methyl center.[20] The reaction with the N^2-butyl derivative **3d** was conducted under the same conditions (KDA, THF, reflux, entry 4), and remarkably, no reaction occurred, including no alkyl shift; hence, aryne formation must have preceded the alkyl shift and is required for the alkyl shift to occur for this particular substrate. Alternatively, this suggests the unexpected possibility that the benzyne formation itself may be dependent upon prior alkyl shift since the *N*,*N*′-dimethyl derivative *did* afford the methyl-shifted phenazine under the same conditions (entry 2). When the reaction was conducted in a sealed vessel at 95 °C (entry 5) apparent alkyl transfer of the butyl group was seen with concomitant formation of the phenazine derivative **5b**. The higher temperature required for the butyl shift is consistent with the rate difference for primary alkyl versus methyl substrates in an S_N2-type reaction.

We considered that the rate of dealkylation in the case of R^2 = CH_3 may be faster than the rate of the benzyne formation (Scheme 2). The deprotonated terminal aniline nitrogen (N^3, structure **11**) should be more basic as well as more nucleophilic than the N^2-dealkylated anilide **12**. Therefore, if a dynamic equilibrium exists wherein the alkyl substituent can shuttle back and forth between N^2 and N^3 (anilides **11** and **12**, Scheme 3), then the equilibrium should shift toward having the anionic charge on N^2 where it enjoys greater stabilization via resonance. This, however, begs the question of why N^1 is not dealkylated as well. The isolated phenazine always bears a methyl on N^1 and is not observed as a mixture of N^1–CH_3 and N^1–H derivatives. However, only N^2 is appropriately spaced to attack the benzyne, and dealkylation of N^1 would be very unlikely after the phenazine formation since the *N*-methyl bond is orthogonal to the π system. The direct transfer of the methyl from N^2 to N^3 (**11a** to **12**) requires an a priori forbidden[25] but occasionally observed[26] *5-endo-tet* mechanism. The transition state for the *5-endo-tet* in this case, however, is essentially an S_N2 reaction from the same face as the leaving group. Alternatively, a Smiles[27] rearrangement (**11b–d**) may occur which would *appear* to proceed via an alkyl shift while actually exchanging N^2 and N^3 along with their respective substituents. The Smiles rearrangement often proceeds with anion-stabilizing groups on the aromatic ring that is attacked, and typically with an exchange of heteroatoms, for example, an N-nucleophile replacing an O-leaving group.

Encouraged by the lack of alkyl shift with R^2 = butyl in our quest for a benzyne approach to the 1,4,7-triazacyclononatriene, we reasoned that if the benzyne could be formed under milder conditions, then N^2 would remain blocked and potentially circumvent 6-membered ring formation. We therefore decided to change the halogen from chlorine to fluorine to enhance the

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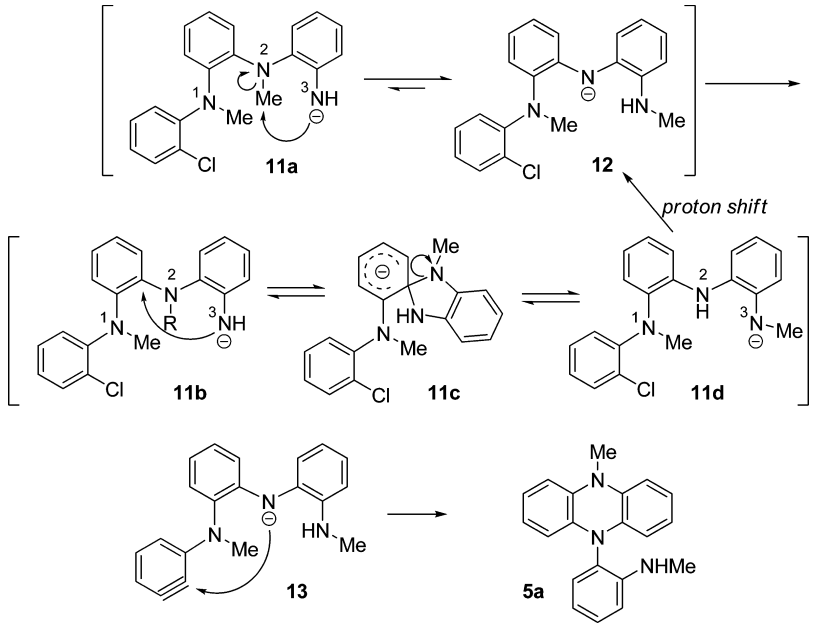
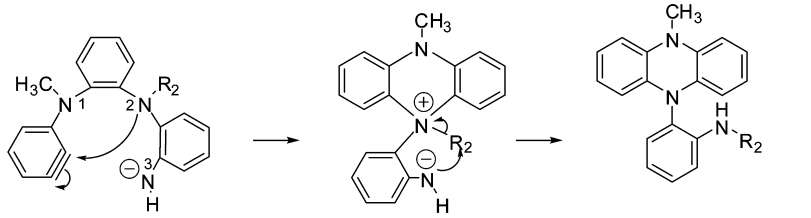
Scheme 3. Possible Mechanism of Alkyl Shift Prior to Phenazine Formation



Scheme 4. Alkyl Shift and Rearrangement via Proposed Zwitterionic Intermediate 14



rate of formation of the aryne as it can stabilize the incipient negative charge on the adjacent carbon.[28,29] Substitution of the chlorine atom with a fluorine atom was accomplished as outlined in Scheme 2, adapted from our earlier reported procedure[9] as described above. Treatment of fluoro aniline substrate **3b** with KDA in refluxing THF afforded a 98% yield of phenazine **5a** (Table 1, entry 3).

The formation of phenazine derivative **5a** employing fluorine as the halogen led us to combine strategies and introduce the *n*-butyl substituent on N^2 as was done for substrate **3d**. When aniline **3e** containing the fluorine and the *n*-butyl group was subjected to KDA in refluxing THF (Table 1, entry 6), the alkyl transfer was once again observed giving rise to phenazine **5b** in 98% isolated yield and suggests that the formation of the benzyne intermediate *precedes* that of the rearrangement. The possible change in the reaction sequence and the isolation of phenazine **5b** suggests the unusual zwitterion **14a/b** as an intermediary (Scheme 4). The zwitterion could be formed from the neutral, tertiary aniline attacking the benzyne intermediate, followed by either an intramolecular alkyl transfer again via a 5-*endo-tet* mechanism, or via intermolecular S_N2 dealkylation. Formation of zwitterions **14a/b** requires attack by a less nucleophilic neutral aniline in the presence of a more nucleophilic anilide, yet the formation of a zwitterion from attack by a neutral nucleophile on an aryne is not without precedent. Kunai and co-workers[30] reported nucleophilic attack on an aryne by an imidazole forming a zwitterion which was neutralized by abstraction of a proton, consistent with our proposed intermediates **14a** and **14b**. Since the internal nitrogen N^2 has no proton to abstract, dealkylation is required to lead to the neutral phenazine derivative. We believe that the alkyl transfer is intramolecular, although labeling experiments would be required to confirm this in the present case. Reactant concentrations were kept intentionally rather low to encourage intramolecular macrocycle formation and to discourage intermolecular processes; the dimethyl chloroaniline **3a** concentration was 0.05 M and the methylbutylchloroaniline **3d** concentration was at 0.03 M, whereas KDA concentrations were kept at 0.17 and 0.16 M in these two reactions, respectively (initial concentrations of DIPA in the presence of excess KH). Phenazines **5a** and **5b** were isolated in high yield in both cases, and we did not isolate any phenazine where the N^2-alkyl group was lost rather than transferred, as would be expected if a slower intermolecular process were competing with dealkylation by KDA in solution. Alternatively, a Smiles rearrangement could precede or even follow aryne formation.

In order to determine if alkyl transfer is dependent on prior benzyne formation, substrates lacking a halogen leaving group were subjected to the identical conditions which were employed for benzyne formation. Nor-halo derivatives **3c** and **3f** were synthesized as outlined in Scheme 2 bearing methyl and *n*-butyl groups on N^2, respectively. When compound **3c** was treated with KDA in refluxing THF, one methyl substituent was apparently transferred from N^2 to the terminal (N^3) aniline

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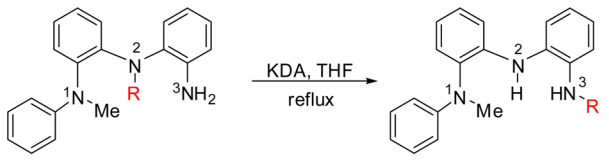
nitrogen affording **15c** in 89% yield (Scheme 5), demonstrating that rearrangement can occur independently of benzyne

Scheme 5. Alkyl Transfer without Benzyne Formation



formation by the action of the nucleophilic terminal anilide (N^3). When anilide **3f** bearing N^1-methyl and N^2-butyl groups but no halogen was subjected to KDA in THF at reflux, the major product isolated in 73% yield was the N^3-butyl derivative **15f**, with the methyl group remaining on the N^1 position. This result is surprising since the angle of attack by the N^3-anilide nitrogen is not ideal for an S_N2 reaction for the proximal N^2-methyl (5-endotrig). This experiment employing aryl substrates lacking a halogen that are unable to form an aryne demonstrates that the apparent alkyl shift can occur without benzyne formation. Furthermore, the N^2-methyl or N^2-*n*-butyl are the groups transferred, as evidenced by upfield ^{13}C shifts of the migrating carbon, and by comparison with calculated ^{13}C spectra utilizing ab initio density functional (DFT) calculation of equilibrium geometry with RB3LYP/6-31G* level of theory (Schemes S1 and S2, Supporting Information).

We believe that the alkyl transfer from N^2 to N^3 in the conversion of **3c/f** to **15c/f** is intramolecular. In the case of the nor-halo substrate **3c**, intermolecular alkyl transfer is very unlikely because a single product is formed in which only one alkyl group is transferred. If the transfer were intermolecular, a mixture of products where either the N^1-methyl or the N^2-methyl were transferred would have been expected, as the two methyl groups of **3c** should have comparable reactivity toward S_N2 displacement given the similar diphenylamine leaving groups. Products from outright loss of alkyl groups from dealkylation by KDA were not isolated.

CONCLUSIONS

It was originally hoped that a benzyne intermediate would provide an efficient route to the targeted 1,4,7-triazacyclononatriene **2a**. Models suggested that overlap of the N^3 anilide with the in-plane benzyne orbital would be ideal for the final cyclization step of the linear synthesis. However, when NMR spectra from the benzyne cyclization reactions commencing with halo derivatives **3** were compared with those of the purified *N*,*N*′-dimethyl-1,4,7-triazacyclononatriene orthocyclophane molecule isolated from Buchwald–Hartwig N-arylation conditions, there was no trace of the 9-membered cyclophane detected in the crude mixtures by ^1H NMR, whereas the apparent alkyl-shifted phenazine derivatives **5a/b** were formed very efficiently, in 78–98% depending on the halogen and alkyl group present. This conversion is dependent upon two factors: the halogen present and the alkyl group employed as the substituent on the internal nitrogen. The evidence provided by these studies suggests the possibility of a neutral N^2 aniline nucleophile attacking the proximal carbon of the aryne affording a zwitterionic intermediate (**14a/b**) followed by an alkyl shift from N^2 to N^3 to afford a phenazine derivative. We envisioned that this may occur via a rare 5-*endo-tet* pathway, although a classic Smiles rearrangement may be more likely since theoretical studies do not support a frontside attack, which would be required in a genuine 5-*endo-tet* process. Specifically, Hase[31] has performed an ab initio (HF/3-21+G*) trajectory study of the S_N2 reaction of $Cl^- + CH_3Cl$ at a reagent relative translational energy of 100 kcal/mol and observed the expected backside attack but no frontside attack and suggested that extensive electrophile vibrational energy would be required for frontside attack. Furthermore, reported 5-*endo-tet* processes[26] are ambiguously categorized since they involve 3-membered ring (generally epoxide) openings under acidic conditions with significant carbocation character and hence are more appropriately categorized as (allowed) 5-*exo-trig* reactions. Indeed, Baldwin noted that three-membered ring-openings lie between tetrahedral and trigonal systems.[25] It may be noted that some confusion arises upon categorization of the cyclizations of a 3,4-epoxybutan-1-ol system to form a tetrahydrofuran, which is an "endo" cyclization (per Baldwin) but could be considered either an allowed 5-*exo-tet* or a disfavored 6-*endo-tet* (counting the oxygen atom of the epoxide as part of the larger ring). As noted, a genuine 5-*endo-tet* pathway would involve attack by a nucleophile at the same face as the leaving group, in opposition to the classic S_N2 trajectory of 180°; thus it is unlikely that the intramolecular alkyl transfer occurs as depicted in Scheme 3 and more likely is the result of a Smiles rearrangement, although the intermediacy of the zwitterionic intermediate (**14a/14b**) remains an intriguing possibility. Labeling experiments would be required to definitely differentiate between these possibilities. Further experiments are underway to study this unusual and theoretically interesting alkyl transfer in more detail.

EXPERIMENTAL SECTION

General Experimental Methods. All solvents were distilled prior to use, and all reagents were used without further purification unless otherwise noted. All Pd-catalyzed and Cu-catalyzed reactions were conducted under an inert atmosphere of argon, and all other reactions were conducted under a nitrogen atmosphere. Silica gel 60A, 40–75 μm (200 × 400 mesh), was used for column chromatography. Aluminum-backed silica gel 200 μm plates were used for TLC. ^1H NMR spectra were obtained uisng a 300 MHz spectrometer with trimethylsilane (TMS) as the internal standard. ^{13}C NMR spectra were obtained using a 75 MHz spectrometer. A 300 W microwave reactor with pressure and temperature sensors was used for all microwave (MW) reactions. Infrared (IR) spectra were determined as a solution in $CHCl_3$. HRMS spectra were measured on a TOF instrument by electrospray ionization (ESI). Single-crystal X-ray diffraction data were collected on a charge-coupled-device (CCD) diffractometer with a liquid nitrogen vapor cooling device. Data were collected at 100 K with graphite-monochromatized MoKα X-ray radiation (λ = 0.71073 Å). Collected and reduced data were corrected for absorption using multiscan methods. The structure was solved by direct methods and refined by full matrix least-squares against F^2 with all reflections. Non-hydrogen atoms were refined anisotropically. C–H hydrogen atom positions were idealized. Additional details of the structure determinations for the tosylate and hydrochloride salts of **5a** can be found in the Supporting Information.

***N*-Methyl-2-(10-methylphenazin-5(10*H*)-yl)aniline (2a).** Similar to the procedure employed by Panagopoulos et al.[9] but under optimized thermal conditions, a 125 mL pressure flask was charged with XPhos (426 mg, 0.89 mmol) and $Pd(dba)_2$ (255 mg, 0.443 mmol), and a solution of compound **3a** (712 mg, 2.11 mmol) in 42 mL of anhydrous 1,4-dioxane was added. The resulting solution was stirred at room temperature for 15 min as argon was passed over the solution. Cesium carbonate (1.38 g, 4.23 mmol) was then added as a solid and the resulting suspension purged with argon for 30 min. The

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flask was then sealed and heated in a 140 °C oil bath for 16 h. The reaction mixture was cooled to room temperature and filtered through a pad of Celite and the filter cake washed with 1:1 methanol/CH_2Cl_2. The filtrate was concentrated to dryness leaving a brown solid which was dissolved in ethyl acetate and the solution passed through a plug of silica gel eluting with 2:1 petroleum ether/CH_2Cl_2. The filtrate was concentrated to dryness leaving a tan powder that was dissolved in CH_2Cl_2. The CH_2Cl_2 solution was purified by flash chromatography eluting with a gradient from 10% CH_2Cl_2/petroleum ether to 33% CH_2Cl_2/petroleum ether to give **2a** (375 mg, 59% yield) as a tan powder, mp 228−230 °C.

***N*^{1}-(2-Aminophenyl)-*N*^{2}-(2-fluorophenyl)-*N*^{1},*N*^{2}-dimethylbenzene-1,2-diamine (3b).** CuCl (137 mg, 1.38 mmol) was added to a stirring solution of the nitroaryl derivative **10b** (164 mg, 0.46 mmol) in dry MeOH (5 mL) at rt. KBH_4 (248 mg, 4.60 mmol) was then added in portions.[21] The reaction effervesced, and a black precipitate formed upon each addition. Once all of the KBH_4 was added, the reaction continued to stir at rt until the solution became clear in color (2−4 h). The reaction was quenched with H_2O and extracted with 3 × 10 mL 90/10 EA/CH_2Cl_2. The organic layers were combined and dried over Na_2SO_4. The solvent was removed under vacuum to give the aniline **3b** as a light brown oil (144 g, 98% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.12 (2H, m), 7.00 (2H, m), 6.92 (3H, m), 6.78 (2H, m), 6.65 (2H, m), 6.56 (1H, dd, J = 9.2, 1.5 Hz), 3.17 (2H, bs), 3.08 (3H, s), 2.97 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.1 (d, J = 270 Hz), 145.2, 141.7, 140.8, 137.4, 137.1, 127.0, 125.6, 124.9, 124.0, 123.5, 122.6, 120.1, 119.9, 119.3, 118.7, 116.4, 116.1, 39.8, 38.4; IR ($CDCl_3$) 3435 (NH_2), 3346 (NH_2), 1612 (C═C), 1501 (NO_2) cm^{-1}; HRMS MH$^+$ calcd for $C_{20}H_{21}N_3F$ 322.1719 found 322.1728.

***N*^{1}-(2-Aminophenyl)-*N*^{1},*N*^{2}-dimethyl-*N*^{2}-phenylbenzene-1,2-diamine (3c).** CuCl (0.297 g, 3 mmol) was added to a stirring solution of the nor-halo dimethyl derivative **10c** (0.212 g, 1.00 mmol) in a 1:1 mixture of dry MeOH and CH_2Cl_2 (20 mL) at rt. KBH_4 (0.540 g, 8.0 mmol) was then added in portions.[21] The reaction effervesced, and a black precipitate formed upon each addition. Once all the KBH_4 was added, the reaction continued to stir at rt until the solution became clear in color and TLC showed consumption of **10c** (2−4 h). The reaction was quenched with H_2O and extracted with 3 × 10 mL 90/10 EA/CH_2Cl_2. The organic layers were combined and dried over Na_2SO_4. The solvent was removed under vacuum to give the *N*,*N*′-dimethyldiphenylamine derivative **3c** as a light brown oil (0.163 g, 96% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (1H, td, J = 6.3, 2.3 Hz), 7.21 (1H, d, J = 4.8 Hz), 7.10 (2H, td, J = 7.0, 1.0 Hz), 7.05−7.04 (2H, m), 6.87 (1H, td, J = 7.5, 1.0 Hz), 6.66 (1H, td, J = 7.5, 1.2 Hz), 6.61−6.58 (3H, m), 6.31 (2H, dd, J = 8.5, 1.0 Hz), 2.99 (2H, br s), 2.97 (3H, s), 2.50 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.8, 147.3, 142.8, 138.7, 138.3, 129.9, 128.6, 126.8, 125.3, 123.9, 122.6, 118.8, 118.6, 116.2, 116.1, 112.3, 38.4, 37.9; HRMS MH$^+$ calcd for $C_{20}H_{22}N_3$ 304.1808, found 304.1808.

***N*^{1}-(2-Aminophenyl)-*N*^{1}-butyl-*N*^{2}-(2-chlorophenyl)-*N*^{2}-methylbenzene-1,2-diamine (3d).** Following the general procedure of Sanz,[21] CuCl (0.060 g, 0.060 mmol) was added to a stirring solution of compound **10d** (0.079 g, 0.2 mmol) in MeOH (2.0 mL) at rt, and then KBH_4 (0.108 g, 2.0 mmol) was added in portions. The reaction stirred at rt until the solution became clear (2−4 h). The reaction was then quenched with H_2O and extracted 3 × 15 mL 90/10 EA/CH_2Cl_2. The organic layers were combined and dried over Na_2SO_4, and the solvent was removed to give the desired aniline **3d** as a brown oil (0.063 g, 82%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (1H, dd, J = 7.8, 1.5 Hz), 7.15−7.00 (4H, m), 6.95−6.84 (5H, m), 6.73−6.62 (2H, m), 3.46 (5H, m), 3.20 (3H, s), 1.42−1.32 (2H, m), 1.25−1.16 (2H, m), 0.82 (3H, t, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.2, 143.3, 143.2, 142.4, 135.8, 131.2, 127.4, 127.3, 125.3, 124.8, 124.5, 123.7, 123.0, 118.4, 116.4, 50.6, 40.3, 30.2, 20.5, 14.1; IR ($CDCl_3$) 3436 (NH_2), 3375 (NH_2), 2956 (C−H), 2929 (C−H), 2869 (C−H), 1491 (C═C) cm^{-1}; HRMS MH$^+$ calcd for $C_{23}H_{27}N_3Cl$ 380.1888, found 380.1892.

***N*^{1}-(2-Aminophenyl)-*N*^{1}-butyl-*N*^{2}-(2-fluorophenyl)-*N*^{2}-methylbenzene-1,2-diamine (3e).** CuCl (47 mg, 0.48 mmol) was added to a stirring solution of nitroaryl derivative **10e** (63 mg, 0.17 mmol) in dry MeOH (2 mL) at rt. KBH_4 (86 mg, 1.6 mmol) was then added in portions.[21] The reaction effervesced, and a black precipitate formed upon each addition. Once all the KBH_4 was added, the reaction continued to stir at rt until the solution became clear in color (2−4 h). The reaction was quenched with H_2O and extracted with 3 × 10 mL 90/10 EA/CH_2Cl_2. The organic layers were combined and dried over Na_2SO_4. The solvent was removed under vacuum to give the aniline derivative **3e** as a light brown oil (60 mg, 100% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18−6.99 (5H, m), 6.95−6.86 (2H, m), 6.78−6.71 (2H, m), 6.66−6.60 (2H, m), 6.50 (1H, ddd, J = 9.6, 8.2, 1.8 Hz), 3.38 (2H, t, J = 7.8 Hz), 3.20 (2H, bs), 2.90 (3H, s), 1.51−1.41 (2H, m), 1.32−1.20 (2H, m), 0.86 (3H, t, J = 7.3 Hz); ^{1}H NMR ($CDCl_3$, 125 MHz) δ 154.2 (d, J = 274 Hz), 145.9, 142.6, 142.1, 137.3, 128.0, 125.8, 125.1, 124.7, 124.2, 121.4, 121.3, 121.0, 119.8, 119.8, 119.4, 118.7, 116.5, 116.3, 50.9, 40.4, 30.0, 20.6, 14.2 ppm; HRMS MH$^+$ calcd for $C_{23}H_{27}N_3F$ 364.2184, found 364.2175.

***N*^{1}-(2-Aminophenyl)-*N*^{1}-butyl-*N*^{2}-methyl-*N*^{2}-phenylbenzene-1,2-diamine (3f).** Compound **10f** (633 mg, 1.69 mmol) was dissolved in 17 mL of dry methanol and the solution stirred at rt. According to the general method of Sanz,[21] to that solution was added CuCl (508 mg, 5.13 mmol) in one portion and stirring was continued for 10 min before KBH_4 (738 mg, 13.7 mmol) was added portionwise maintaining the reaction temperature below 30 °C. The reaction mixture was stirred at ambient temperature under nitrogen atmosphere for 2.5 h. The reaction was then quenched via the addition of water and then was extracted 3× with ethyl acetate. The organic extracts were combined, dried over $MgSO_4$, and filtered, and the filtrate was concentrated to dryness leaving a brown gum that was purified by flash chromatography eluting with an eluent comprised of 3% ether, 5% CH_2Cl_2 and 92% petroleum ether to give triaryl derivative **3f** (202 mg, 25% yield, two steps) as a brown oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29−7.26 (1H, m), 7.13 (1H, d, J = 8.0 Hz), 7.08 (1H, t, J = 11.0 Hz), 7.05−7.01 (2H, m), 6.86−6.83 (1H, m), 6.66 (1H, t, J = 7.0 Hz), 6.60−6.54 (2H, m), 6.32 (1H, s), 6.30 (1H, s), 3.27 (2H, t, J = 8.0 Hz), 2.99 (2H, bs), 2.46 (3H, s), 1.61−1.55 (4H, m), 1.30 (2H, q, J = 7.5 Hz), 0.99 (3H, t, J = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.3, 146.2, 143.1, 139.8, 138.3, 130.3, 128.5, 126.5,125.0, 124.7, 122.7, 119.7, 118.5, 116.2, 116.0, 112.4, 50.6, 37.9, 29.8, 20.4,14.0; HRMS MH$^+$ calcd for $C_{23}H_{28}N_3$ 346.2278, found 346.2279.

***N*-Methyl-2-(10-methylphenazin-5(10*H*)-yl)aniline (5a).** In an oven-dried round-bottom flask was washed KH (0.543 g, 4.06 mmol) with dry petroleum ether (3 × 5 mL) under N_2 at rt, and 1 mL of THF was added to the KH and stirred at rt for 5 min. Diisopropylamine (0.15 mL, 1.0 mmol) was then added to the KH and the mixture stirred at rt for 5 min. Compound **3a** (0.098 g, 0.29 mmol) in THF (5 mL) was added dropwise by syringe to the KDA in THF (1 mL). The mixture was heated to reflux for 1−2 h until TLC showed complete consumption of **3a**. The reaction mixture was quenched with 15 mL of H_2O and extracted 3 × 20 mL of Et_2O. The organic layers were combined and dried over $MgSO_4$, and the solvent was removed in vacuo to yield phenazine **5a** as a colorless solid (80 mg, 92%): mp 202−204 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (1H, ddd, J = 9.2, 7.8, 1.5 Hz), 7.16 (1H, dd, J = 8.1, 1.5 Hz), 6.82 (2H, t, J = 15.7, 7.8 Hz), 6.63 (2H, ddd, J = 9.1, 7.7, 1.4 Hz), 6.41 (2H, ddd, J = 8.7, 7.8, 1.2 Hz), δ 6.34 (2H, dd, J = 7.7, 1.1 Hz), δ 5.82 (2H, dd, J = 7.8, 1.2 Hz), δ 4.45 (1H, bs), 3.01 (3H, s), 2.79 (3H, bs); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.9, 136.9, 131.1, 129.6, 129.2, 125.5, 121.7, 120.7, 117.5, 111.8, 111.2, 110.9, 30.2, 29.7; HRMS M$^+$ calcd for $C_{20}H_{20}N_3$ 301.1573, found 301.1562. The desired product was then dissolved in 2−3 mL of Et_2O, and 1 equiv of *p*-toluenesulfonic acid was added to form the tosylate salt as clear crystals suitable for X-ray crystallography. Similarly, addition of HCl/ether to **5a** in Et_2O afforded the hydrochloride salt as clear crystals suitable for X-ray crystallography.

***N*-Butyl-2-(10-methylphenazin-5(10*H*)-yl)aniline (5b).** In a round-bottom flask, 2 mL of THF and DIPA (0.11 mL, 0.80 mmol) were added to KH (0.300 g, 2.24 mmol) at rt. The mixture was stirred for 10 min, and aniline **3e** (58 mg, 0.16 mmol) in 3 mL of THF was added dropwise via syringe. The reaction mixture was heated to reflux

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for 2 h. The reaction mixture was cooled to rt and quenched with H_2O. The product was extracted with 3 × 20 mL of 90/10 EA/CH_2Cl_2. The organic layers were combined and dried over Na_2SO_4, and the solvent was removed under reduced pressure to give the phenazine derivative **5b** as a green oil (0.048 g, 87% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.3 (1H, ddd, J = 8.5, 7.3, 2.3), 7.16, (1H, dd, J = 7.7, 1.4), 6.83−6.75 (2H, m), 6.62 (2H, t, J = 7.7), 6.41 (1H, t, 7.7), 6.34 (1H, d, J = 7.8), 5.81 (2H, dd, J = 7.8, 1.2), 4.37 (1H, bs), 3.12 (2H, t, J = 7.1), 3.02 (3H, s), 1.55−1.43 (2H, m), 1.36−1.21 (2H, m), 0.85 (3H, t, J = 7.3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.2, 131.5, 129.7, 121.9, 121.1, 117.7, 112.2, 112.0, 111.1, 43.3, 31.6, 29.9, 20.3, 14.0 (all aromatic carbons peaks are broadened due to hindered rotation except for 129.7, while the aliphatic carbon resonances are sharp); IR ($CDCl_3$) 3415 (NH), 2965 (C−H), 2962 (C−H), 2870 (C−H), 1607 (C═C), 1508 (C═C), 1482 (C═C) cm^{-1}; HRMS M$^+$ calcd for $C_{23}H_{26}N_3$ 343.2043, found 343.2046.

(2′-Fluorophenyl)-(2-nitrophenyl)-amine (6b). (2′-Fluorophenyl)-(2-nitrophenyl)amine **6b** was synthesized according to the general procedures outlined by Tietze et al.[23] A pressure tube was charged with o-nitroaniline (0.690 g, 5.00 mmol), *o*-fluoroiodobenzene (0.70 mL, 6 mmol), $Pd(dba)_2$ (0.144 g, 5%), BINAP (0.233 g, 7.5%), Cs_2CO_3 (3.26 g, 10 mmol), and toluene (10 mL). The mixture was purged with argon for 10 min at rt, and the pressure tube was sealed. The reaction was placed in an oil bath. The temperature was brought to 120 °C and the reaction stirred for 24 h. TLC showed complete consumption of *o*-nitroaniline, and the reaction mixture was filtered through a pad of SiO_2 using 10/90 CH_2Cl_2/EA as the eluent. The solvent was removed under reduced pressure and product was purified by column chromatography using 1/99 Et_2O/petroleum ether as the eluent to afford the final product **6b** as orange crystals (0.915 g, 78% yield): mp 79−80 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.31 (1H, br s), 8.24 (1H, dd, J = 8.7, 1.5 Hz), 7.44−7.37 (2H, m), 7.24−7.18 (3H, m), 7.08 (1H, dt, J = 2.9, 1.5, 1.4 Hz), 6.83 (1H, ddd, J = 7.2, 7.0, 1.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.6 (d, J = 248 Hz), 142.2, 139.4, 135.7, 130.1, 126.8, 125.9, 124.7, 118.1, 116.8, 116.7, 116.0; IR ($CDCl_3$) 3345 (NH), 1609 (C═C), 1577 (C═C), 1509 (NO_2) cm^{-1}; HRMS (M + H)$^+$ calcd for $C_{12}H_{10}N_2O_2F$ 233.0721, found 233.0727.

2-Nitro-*N*-phenylaniline (6c). 2-Nitro-*N*-phenylaniline **6c** was synthesized according to the general procedures outlined by Tietze et al.[23] A pressure tube was charged with *o*-nitroaniline (1.38 g, 10 mmol), bromobenzene (1.2 mL, 10 mmol), $Pd(dba)_2$ (0.288 g, 5%), BINAP (0.466 g, 7.5%), Cs_2CO_3 (6.52 g, 20 mmol), and toluene (20 mL). The mixture was purged with argon for 10 min at rt and the pressure tube was sealed. The reaction was placed in an oil bath. The temperature was brought to 120 °C, and the reaction stirred for 48 h. TLC showed complete consumption of *o*-nitroaniline and the reaction mixture was filtered through a pad of silica gel using 5/5/90 EA/CH_2Cl_2/petroleum ether as the eluent. The filtrate was dried over Na_2SO_4 and the solvent removed under reduced pressure to give the desired 2-nitro-*N*-phenylaniline **6c** as an orange solid without further purification (2.08 g, 98% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.48 (1H, bs), 8.19 (1H, dd, J = 8.7, 1.8 Hz), 7.43 (1H, d, J = 1.8 Hz), 7.41−7.32 (2H, m), 7.28−7.23 (4H, m), 6.76 (1H, dd, J = 1.8, 1.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.9, 138.6, 135.5, 133.0, 129.6, 126.5, 125.5, 124.2, 117.4, 115.9.

2-Fluoro-*N*-methyl-*N*-(2-nitrophenyl)aniline (7b). To a solution of aniline **6b** (0.122 g, 0.525 mmol) in acetone (2 mL) at rt was added freshly crushed KOH (0.130 g, 2.31 mmol). The reaction was heated to reflux, and Me_2SO_4 (0.23 mL, 2.42 mmol) was added dropwise via syringe. The mixture was allowed to reflux for 1 h. The reaction was cooled to rt, and 1 mL of 10 M NaOH was added to the solution. After 1 h, the mixture was quenched with 2 mL H_2O and extracted with 3 × 10 mL of 90/10 EA/CH_2Cl_2. The organic layers were combined and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the mixture was placed in an 80 °C oil bath under vacuum to remove excess Me_2SO_4 providing fluoronitrobenzene derivative **7b** as a brown oil (0.122 g, 95% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (1H, dd, J = 7.8, 1.7 Hz), 7.5 (1H, ddd, J = 8.2, 7.4, 1.7 Hz), 7.24 (1H, dd, J = 8.4, 1.2 Hz), 7.09−6.94 (5H, m), 3.33 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.6 (d, J = 255 Hz), 142.5, 138.9, 136.9, 126.9, 125.7, 125.4, 122.6, 120.8, 119.3, 117.2, 116.5, 41.1; IR ($CDCl_3$) 1522 (NO_2), 1501 (NO_2) cm^{-1}; HRMS (M + H)$^+$ calcd for $C_{13}H_{11}N_2O_2F$ 247.0877, found 247.0871.

***N*-Methyl-2-nitro-*N*-phenylaniline (7c).** To a solution of aniline **6c** (0.182 g, 1.0 mmol) in DMF (5 mL) at rt was added freshly crushed KOH (0.252 g, 4.5 mmol). After 10 min, MeI (0.20 mL, 3 mmol) was added to the stirring mixture dropwise via syringe. Stirring was continued at rt until TLC showed consumption of the aniline starting material. The reaction was then quenched with 25 mL of deionized H_2O and extracted with 3 × 30 mL of EA. The organic layers were combined and dried over $MgSO_4$. The solvent was removed under reduced pressure and no further purification was needed to obtain the nor-halo *N*-methyl derivative **7c**[24] as a brown oil (0.194 g, 100% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (1H,dd,J = 8.1, 1.5 Hz), 7.57 (1H,dt, J = 8.6, 1.8 Hz), 7.35 (1H, dd, J = 8.1, 1.5 Hz), 7.27 (2H, dt, J = 15.4, 1.5 Hz), 7.21 (2H, dt, J = 8.1, 1.5 Hz), 6.83 (1H, dt, J = 7.2, 1.2 Hz), 6.72 (1H, dt, J = 7.2, 1.2 Hz), 3.31 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.8, 146.3, 142.2, 133.8, 129.2, 129.1, 125.6, 125.0, 119.9, 115.6, 40.2.

***N*^{1}-(2-Fluorophenyl)-*N*^{1}-methylbenzene-1,2-diamine (8b).** CuCl (0.150 g, 1.50 mmol) was added to a stirring solution of fluoro nitrobenzene derivative **7b** (0.122 g, 0.5 mmol) in dry MeOH (5.0 mL) at rt. KBH_4 (0.270 g, 5.0 mmol) was then added in portions.[21] The reaction effervesced, and a black precipitate formed upon each addition. Once all the KBH_4 was added, the reaction continued to stir at rt until the solution became clear in color (2−4 h). The reaction was quenched with H_2O and extracted with 3 × 10 mL 90/10 EA/CH_2Cl_2. The organic layers were combined and dried over Na_2SO_4. The solvent was removed under vacuum to give the desired fluoro aniline **8b** as a light brown oil (0.096 g, 89% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.06−6.85 (6H, m), 6.76 (1H,dd, J = 7.8, 1.2 Hz), 6.70 (1H, ddd, J = 8.8, 7.7, 1.4 Hz), 3.91 (2H, bs), 3.15 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.9 (d, J = 240 Hz), 142.1, 138.6, 136.8, 126.1, 124.5 (d, J = 37 Hz), 121.7, 119.6, 118.8, 116.4, 116.1, 115.8, 34.0; IR ($CDCl_3$) 3452 (NH_2), 3351 (NH_2), 1608 (C═C), 1500 (C═C) cm^{-1}; HRMS MH$^+$ calcd for $C_{13}H_{14}N_2F$ 217.1136, found 217.1133.

***N*^{1}-Methyl-*N*^{1}-phenylbenzene-1,2-diamine (8c).** CuCl (0.297 g, 3 mmol) was added to a stirring solution of the nor-halo *N*-methyl derivative **7c** (0.208 g, 1.00 mmol) in dry MeOH (10 mL) at rt. KBH_4 (0.540 g, 8.0 mmol) was then added in portions.[21] The reaction effervesced and a black precipitate formed upon each addition. Once all the KBH_4 was added, stirring was continued at rt until the solution became clear in color and TLC showed consumption of **7c** (2−4 h). The reaction was quenched with H_2O and extracted with 3 × 10 mL 90/10 EA/CH_2Cl_2. The organic layers were combined and dried over Na_2SO_4. The solvent was removed under vacuum to give the N-methyl diphenylamine derivative **8c**[24] as a light brown oil (0.163 g, 96% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19 (2H, dt, J = 5.4, 1.8 Hz), 7.07 (1H, dt, J = 7.8, 1.5 Hz), 7.03) 1H, dd, J = 7.8, 1.5 Hz), 6.80−6.72 (3H, m), 6.66 (1H, s), 6.63 (1H, s), 3.77 (2H, bs), 3.19 (3H,s).

***N*^{1}-(2-Fluorophenyl)-*N*^{1}-methyl-*N*^{2}-(2-nitrophenyl)benzene-1,2-diamine (9b).** The fluoroaniline derivative **8b** (0.096 g, 0.44 mmol), *o*-iodonitrobenzene (0.132 g, 0.53 mmol), $Pd(dba)_2$ (0.013 g, 5% mol), BINAP (0.021 g, 7.5% mol), Cs_2CO_3 (0.215 g, 0.66 mmol), and 2 mL of toluene were placed in a pressure tube. The mixture was purged with argon at rt for 15 min. The pressure tube was then sealed and placed in a preheated oil bath at 130 °C for 24 h. When TLC showed consumption of **8b**, the reaction mixture was filtered through a pad of SiO_2 eluting with 90/10 EA/CH_2Cl_2. The solvent was removed under reduced pressure, and the resulting product was purified by column chromatography eluting with 1/99 Et_2O/petroleum ether to afford the *N*,*N*′-diarylphenylenediamine derivative **9b** as a red oil (0.082 g, 55% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.12 (1H, bs), 8.05 (1H, dd, J = 8.5, 1.7 Hz), 7.34−7.05 (6H, m), 6.86−6.83 (4H, m), 6.69 (1H, ddd, J = 8.5, 7.1, 1.4 Hz), 3.21 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.3 (d, J = 240 Hz), 144.4, 142.3, 137.8, 135.1, 133.4, 132.5, 126.4, 125.7, 124.2, 123.7, 123.5, 122.7, 122.4, 117.1, 116.4, 116.1, 115.8, 40.6; IR ($CDCl_3$) 3343 (NH), 1615 (C═C),

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1593 (C═C), 1573 (C═C), 1501 (NO_2) cm^{-1}; HRMS MH^+ calcd for $C_{19}H_{17}N_3O_2F$ 338.1299, found 338.1306.

N^1-Methyl-N^2-(2-nitrophenyl)-N^1-phenylbenzene-1,2-diamine (9c). Nor-halo aniline derivative **8c** (0.163 g, 2.5 mmol), *o*-iodonitrobenzene (0.249 g, 2.50 mmol), $Pd(dba)_2$ (0.072 g, 5% mol), BINAP (0.112 g, 7.5% mol), Cs_2CO_3 (0.900 g, 2.75 mmol), and 5 mL of toluene were placed in a pressure tube. The mixture was purged with argon at rt for 15 min. The pressure tube was then sealed and placed in a preheated oil bath at 120 °C for 36 h. When TLC showed consumption of **8c**, the reaction mixture was filtered through a pad of silica gel eluting with 90/10 EA/CH_2Cl_2. The solvent was removed under reduced pressure and the resulting product was purified by column chromatography eluting with 10/90 EA/petroleum ether to afford the desired dimethyl derivative **9c** as a yellow gum (0.163 g, 70% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.24 (1H, s), 8.08 (1H, dd, J = 9.9, 1.8 Hz), 7.47−7.43 (1H, m), 7.34−7.20(5H, m), 7.11 (2H, dt, J = 6.4, 1.0 Hz), 6.74 (2H,ddd, J = 7.5, 7.9, 1.2 Hz), 6.65 (1H, d, J = 1.0 Hz), 6.62 (1H, d, J = 1.0 Hz), 3.23 (3H, s); ^{13}C NMR (75 MHz, CDCl3) δ 148.6, 142.1, 141.8, 135.6, 135.12, 133.9, 129.0, 127.8, 126.6, 126.0, 125.9, 123.7, 119.1, 117.7, 116.1, 115.1, 39.6; HRMS MH^+ calcd for $C_{19}H_{18}N_3O_2$ 320.1394, found 320.1394.

N^1-(2-Fluorophenyl)-N^1,N^2-dimethyl-N^2-(2-nitrophenyl)-benzene-1,2-diamine (10b). A solution of fluoro nitroaryl derivative **9b** (0.082 g, 0.24 mmol) in 2 mL of DMF was added to KH (0.100 g, 0.72 mmol, freshly washed with petroleum ether). Upon addition, the solution changed color from orange to deep purple. The mixture was stirred at rt for 10 min, then methyl iodide (1.0 mL, 1.2 mmol) was added dropwise via syringe. Stirring was continued until the solution became bright yellow in color (2 h). The reaction was then quenched with H_2O and extracted with 3 × 10 mL 90/10 EA/CH_2Cl_2. The organic layers were combined and washed with 3 × 20 mL H_2O and then brine. The organic layer was dried over Na_2SO_4, and the solvent was removed under reduced pressure to give the desired N^1,N^2-dimethyl derivative **10b** as a yellow solid (0.082 g, 97% yield): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (1H, dd, J = 8.2, 1.7 Hz), 7.34 (1H, ddd, J = 8.8, 7.4, 1.9 Hz), 7.1−6.75 (10H, m), 3.22 (3H, s), 3.14 (3H, s); ^{13}C NMR (125 MHz, CDCl3) δ 155.1 (d, J = 148 Hz), 143.0, 143.8, 140.9, 137.6, 132.9, 132.6 (d, J = 25 Hz), 125.9, 125.8, 125.6, 125.1, 125.0, 124.4 (d, J = 2 Hz), 122.1 (d, J = 5 Hz), 121.7, 121.5 (d, J = 2 Hz), 120.0, 116.5 (d, J = 12 Hz), 40.1, 39.2; IR ($CDCl_3$) 1606 (C═C), 1591 (C═C), 1568 (C═C), 1522 (NO_2), 1500 (NO_2) cm^{-1}; HRMS $(M + H)^+$ calcd for $C_{20}H_{19}N_3O_2F$ 352.1456, found 352.1463.

N^1,N^2-Dimethyl-N^1-(2-nitrophenyl)-N^2-phenylbenzene-1,2-diamine (10c). To a solution of aniline **9c** (0.163 g, 2.0 mmol) in DMF (10 mL) at rt was added freshly crushed KOH (0.504 g, 9 mmol). After 10 min, MeI (0.40 mL, 6 mmol) was added to the stirring mixture dropwise via syringe. Stirring was continued at rt until TLC showed consumption of the aniline starting material. The reaction was then quenched with 25 mL deionized water and extracted with 3 × 30 mL of EA. The organic layers were combined and dried over $MgSO_4$. The solvent was removed under reduced pressure to provide the nor-halo *N*,*N*′-dimethyl derivative **10c** as a brown oil (0.170 g, 100% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (1H, dd, J = 8.2, 1.6 Hz), 7.29−7.15 (3H, m), 7.11−7.04 (4H, m), 6.92 (1H, dt, J = 7.2, 1.2 Hz), 6.76 (1H, dd, J = 8.2, 1.2 Hz), 6.72 (1H, dt, J = 13.5, 1.2 Hz), 6.34 (1H, d, J = 3.2 Hz), 6.31 (1H, d, J = 1.9 Hz), 3.27 (3H, s), 2.82 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.8, 144.1, 143.5, 142.9, 140.1, 132.8, 129.0, 128.4, 126.5, 125.3, 124.7, 124.4, 123.6, 121.5, 117.5, 113.9, 41.2, 38.1; HRMS MH^+ calc for $C_{20}H_{20}N_3O_2$ 334.1550, found 334.1547.

N^1-Butyl-N^2-(2-chlorophenyl)-N^2-methyl-N^1-(2-nitrophenyl)-benzene-1,2-diamine (10d). A solution of chloro N^1-methylaniline derivative **9a**[9] (0.100 g, 0.28 mmol) in 2 mL of DMF was added to KH (0.112 g, 0.830 mmol). Upon addition, the solution went from orange to deep purple. The mixture was stirred at rt for 10 min. *n*-Butyl bromide (0.30 mL, 2.8 mmol) was added dropwise via syringe. The reaction was warmed to 80 °C and stirred until the solution returned to an orange color (3 h). The reaction was then quenched with H_2O and extracted with 3 × 15 mL EA. The organic layers were combined and washed with 3 × 25 mL of H_2O, brine, then again with H_2O to remove excess DMF. The organic layer was then dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography using a gradient of EA/petroleum ether as the eluent to give the desired product **10d** as a red oil (0.065 g, 56%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (1H, dd, J = 8.0, 1.7 Hz), 7.40 (1H, ddd, J = 8.7, 7.2, 1.6 Hz), 7.24 (1H, dd, J = 15.4, 1.4 Hz), 7.21 (1H, dd, J = 14.8, 1.7 Hz), 7.06 (1H, dd, J = 8.1, 1.5 Hz), 7.02−6.87 (6H, m), 6.76 (1H, dd, J = 8.2, 1.7 Hz), 3.77 (2H, t, J = 8.1 Hz), 3.31 (3H, s), 1.6 (2H, m), 1.29 (2H, m), 0.90 (3H, t, J = 7.4, 7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.7, 132.8, 132.3, 131.0, 130.1, 128.4, 128.3, 127.8, 127.5, 126.3, 125.9, 125.8, 124.1, 124.0, 123.7, 120.7, 120.6, 119.1, 49.8, 38.6, 29.0, 20.1, 14.0 IR ($CDCl_3$) 2958 (C−H), 2929 (C−H), 2871 (C−H), 2817 (C−H), 1524 (NO_2) cm^{-1}; HRMS MH^+ calcd for $C_{23}H_{25}N_3O_2Cl$ 410.1630, found 410.1640.

N^1-Butyl-N^2-(2-fluorophenyl)-N^2-methyl-N^1-(2-nitrophenyl)-benzene-1,2-diamine (10e). A solution of the fluoro nitroaryl derivative **9b** (0.102 g, 0.300 mmol) in 2 mL of DMF was added to KH (0.121 g, 0.910 mmol). Upon addition, the solution went from orange to deep purple. The mixture was stirred at rt for 10 min. *n*-Butyl bromide (0.32 mL, 3.0 mmol) was added dropwise via syringe. The reaction was heated to 80 °C and stirred until the solution returned to an orange color 3 h. The reaction was then quenched with H_2O and extracted with 3 × 15 mL DCM. The organic layers were combined and washed with 3 × 25 mL H_2O, with brine and then with H_2O again to remove excess DMF. The organic layer was then dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography using a gradient of EA/petroleum ether as the eluent to produce the N^1-methyl-N^2-butyl derivative **10e** as a red oil (0.063 g, 53%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (1H, dd, J = 8.1, 1.5 Hz), 7.34 (1H, ddd, J = 8.7, 7.3, 1.7 Hz), 7.11−6.77 (9H, m), 3.59 (2H, t, J = 15.9, 8.0 Hz), 3.06 (3H, s), 1.65−1.54 (2H, m), 1.30 (2H, s, J = 7.3 Hz), 0.88 (3H, t, J = 7.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.4 (d, J = 255 Hz), 141.8, 141.0, 137.5, 132.6, 132.3, 132.0, 130.1, 129.3 (d, J = 30 Hz), 128.3, 127.8, 125.8, 125.6, 125.1, 124.1, 122.6, 121.3, 120.8, 120.3, 116.3 (d, J = 22 Hz), 52.5, 39.2, 29.7, 20.3, 13.9; HRMS MH^+ calcd for $C_{23}H_{25}N_3O_2F$ 394.1925, found 394.1939.

N^1-Butyl-N^2-methyl-N^1-(2-nitrophenyl)-N^2-phenylbenzene-1,2-diamine (10f). Nitro triaryl compound **9c** (735 mg, 2.30 mmol) was placed in a round-bottom flask, and 12 mL of anhydrous DMF was added. To that solution was added powdered KOH (593 mg, 10.6 mmol) and the reaction mixture stirred for 10 min at rt. Then, *n*-butyl bromide (3.21 g, 23.4 mmol) was added neat, and the reaction mixture was heated in an 80 °C oil bath for 3 h. The reaction mixture was then cooled to rt, diluted with 20 mL water, and extracted 3 × with diethyl ether. The organic extracts were combined, dried over $MgSO_4$, and filtered and the filtrate concentrated to dryness to give the *N*-butyl derivative **10f** as a brown oil that was carried on directly without further purification.

N^1-Methyl-N^2-(2-(methylamino)phenyl)-N^1-phenylbenzene-1,2-diamine (15c). A round-bottom flask was charged with 30% KH (187 mg, 1.4 mmol), and the solid was washed under nitrogen atmosphere with 3 × 5 mL portions of petroleum ether. The solid was then suspended in 1 mL anhydrous THF and stirred at RT while diisopropylamine (50.0 μL, 0.356 mmol) was added. Stirring at ambient temperature was continued for 10 min before *N*,*N*′-dimethyl triaryl derivative **3c** (30 mg, 0.10 mmol) was added as a solution in 1 mL of THF. The reaction mixture was then heated and maintained at reflux for 2 h and then cooled to rt. The reaction mixture was diluted with water and extracted 2× with ethyl acetate. The organic extracts were combined, dried over $MgSO_4$, and filtered, and the filtrate was concentrated to dryness. The residue was dissolved in petroleum ether and purified by passing the solution through silica gel eluting with petroleum ether and then with 2% dichloromethane, 10% ether, 88% petroleum ether. The purified material was concentrated to dryness to give the product **15c** as a clear gum (26.8 mg, 89%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (2H, t, J = 7.5 Hz), 7.13−7.07 (4H, m), 6.80 (2H, t, J = 7.5 Hz), 6.80 (2H, t, J = 7.5 Hz), 6.71 (2H, t, J = 4 Hz), 6.65 (3H, t, J = 3.0 Hz), 5.51 (1H,s), 4.06 (1H, bs), 3.29 (3H, s), 2.76

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(3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.3, 146.0, 143.3, 135.0, 129.4, 128.0, 127.6, 127.4, 126.8, 125.9, 119.5,1 18.4, 117.0, 114.1, 114.0, 110.5, 39.4, 30.7; HRMS MH^+ calcd for $C_{20}H_{22}N_3$ 304.1802, found 304.1802.

***N*^{1}-(2-(Butylamino)phenyl)-*N*^{2}-methyl-*N*^{2}-phenylbenzene-1,2-diamine (15f).** A round-bottom flask was charged with 30% KH (374 mg, 2.80 mmol), and the solid was washed with three portions of petroleum ether under nitrogen atmosphere. The solid was then suspended in 1 mL of anhydrous THF, and to that suspension was added distilled diisopropylamine (100 μL, 0.714 mmol). Stirring at ambient temperature was continued for 10 min before a solution of triarylaniline **3f** (69 mg, 0.2 mmol) in 3 mL THF was added. The reaction mixture was then heated and maintained at reflux for 2 h before being cooled to rt. The reaction mixture was diluted with water and extracted 2× ethyl acetate. The organic extracts were combined, dried over $MgSO_4$, and filtered and the filtrate concentrated to dryness. The residue was purified using flash chromatography eluting with 1% dichloromethane, 5% ether, 94% petroleum ether to give the product **15f** as a pale yellow gum (50.3 mg, 73%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (1H, d, J = 1.0 Hz), 7.21 (1H, d, J = 1.0 Hz), 7.12−7.07 (4H, m), 6.79 (2H, dt, J = 7.0, 1.0 Hz), 6.72−6.64 (5H, m), 5.54 (1H, bs), 3.99 (1H, bs), 3.30 (3H, s), 3.04 (2H, t, J = 7.0 Hz), 1.46 (2H, q, J = 7.5 Hz), 1.28 (2H, dq, J = 7.5, 1.0 Hz), 0.90 (3H, t, J = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.9, 143.1, 134.6, 129.2, 127.7, 127.4, 127.0, 126.5, 125.8, 119.1, 118.1, 116.6, 113.7, 113.7, 110.7, 43.4, 39.1, 31.6, 20.3, 13.9; HRMS MH^+ calcd for $C_{23}H_{28}N_3$ 346.2278, found 346.2276.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of spectral data (^{1}H NMR, ^{13}C NMR, IR, and HRMS), details of X-ray crystal structure determination, coordinates, and files for the tosylate and chloride salts of compound **5a** (CIF). ORTEP-style representation for the chloride salt of compound **5a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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