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Ni-catalyzed Iterative Alkyl Transfer from Nitrogen Enabled by the In Situ Methylation of Tertiary Amines

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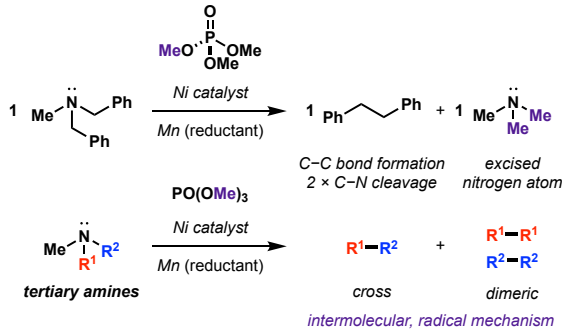
Ni-catalyzed deaminative transforms; iterative alkyl transfer from nitrogen



ABSTRACT: Current methods to achieve transition-metal-catalyzed alkyl C–N bond cleavage require the preformation of ammonium, pyridinium or sulfonamide derivatives from the corresponding alkyl amines. These activated substrates permit C–N bond cleavage and their resultant intermediates can be intercepted to affect C–C bond forming transforms. Here we report the combination of in situ amine methylation and Ni-catalyzed benzalkyl C–N bond cleavage under reductive conditions. This method permits iterative alkyl group transfer from tertiary amines and demonstrates a deaminative strategy for the construction of Csp^3–Csp^3 bonds. We demonstrate $PO(OMe)_3$ (trimethylphosphate) to be a Ni-compatible methylation reagent for the *in situ* conversion of trialkyl amines into tetraalkylammonium salts. Single, double, and triple benzalkyl group transfers can all be achieved from the appropriately substituted tertiary amines. Transformations developed herein proceed via recurring events: the *in situ* methylation of tertiary amines by $PO(OMe)_3$, Ni-catalyzed C–N bond cleavage and concurrent Csp^3–Csp^3 bond formation.

1. INTRODUCTION

1.1. Background. Given the abundance of nitrogen present within chemical feedstocks,[1] pharmaceuticals,[2] and natural products,[3] methods to construct carbon–carbon (C–C) bonds from amines via selective carbon–nitrogen (C–N) bond cleavage processes—where the nitrogen atom is retained (rearranged)[4] or excised[5]—would be of high value for complex molecule synthesis and chemical diversification strategies. Indeed, multistep syntheses that incorporate a Stevens rearrangement, a strategic and predictable C–N bond cleavage method, exemplify the power of nitrogen atom rearrangement chemistry for Csp^3–Csp^3 bond formation.[6] Despite the considerable understanding of C–N bond cleavage reactions,[7] nitrogen atom excision processes that occur with transition metal mediated functionalization of the cleaved C–N bond are known to a lesser extent.[8,9] Certainly, metal-catalyzed hydrodenitrogenation (HDN) processes serve to remove nitrogen atoms from petroleum feedstocks; however, the high temperatures and pressures are generally viewed as non-translatable for precise transformations in a more complex setting.[10] Recent studies using transition-metal catalysis have described the reactivity of amine derivatives as the electrophilic carbon-based partners (R^1) in cross-coupling reactions (**Figure 1a**).[8,9] In particular, *N*-aryl trimethylammonium (R^1 = aryl),[9b-e,11,12] *N*-benzalkyl trimethylammonium (R^1 = benzalkyl)[9e,13,14] and *N*-alkyl pyridinium (R^1 = alkyl) salts[15] have been employed for the selective metal-catalyzed transfer of aryl, benzyl and alkyl groups from nitrogen, respectively. Additionally, visible light mediated methods for alkyl C–N bond cleavage from *N*-benzalkyl trimethylammonium[16] and *N*-alkyl pyridinium salts (R^1 = alkyl) have also been reported.[17]

The practical advantages of ammonium and pyridinium substrates as stable carbon transfer reagents (R^1), include their ready availability from amine precursors,[15a] and if necessary, their facile enantioenrichment by recrystallization.[9e] Moreover, recent strategies have highlighted the latent advantage of tertiary amines employed through multistep sequences to direct electrophilic aromatic substitution[9c,12b] or C–H functionalization chemistries[13e,18] prior to their stepwise removal by quaternization (*e.g.,* permethylation) and chemoselective C–N bond cleavage.

Despite these advances, and the varied mechanisms proposed for C–N bond cleavage, known carbon group transfer reactions (*e.g.*, R^1) from a nitrogen atom occur as singular events (**Figure 1a**). In such reactions, only one group is cleaved (*e.g.,* R^1) and reacted with a nucleophilic partner (R^2). These steps can be mediated by a transition metal to facilitate subsequent cross-coupling to yield products of type R^1–R^2.

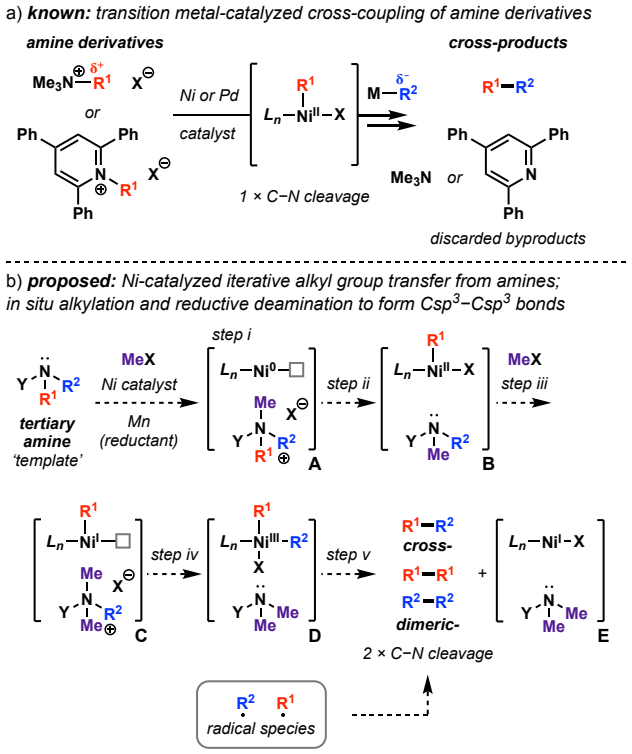


Figure 1. Transition metal-catalyzed cleavage and functionalization of carbon–nitrogen (C–N) bonds.

Similar visible light mediated processes that are proposed to generate and intercept alkyl radical intermediates have also been studied.[16,17] In most cases, the trimethylamine or 2,4,6-triphenylpyridine byproduct is discarded.[16] Thus, the utility of tertiary amines and their corresponding ammonium derivatives in multi-step transforms is underexplored.

1.2. Proposed strategy for iterative alkyl transfer from nitrogen. A fundamental understanding of iterative alkyl group transfer from nitrogen would significantly distinguish alkylammonium substrates from their alkyl halide and alkyl pyridinium counterparts. Theoretically, alkyl amines could permit iterative group transfers via alkyl ammonium intermediates, enabling up to three C–N bond cleavages from a tertiary amine, whereas alkyl halides or alkyl pyridiniums can only affect single group transfer, one C–X or C–N bond cleavage, respectively (**Figure 1a**).

Accordingly, we proposed that tertiary amines could serve to template the programmed construction of Csp^3–Csp^3 bonds with the net excision of a nitrogen atom (**Figure 1b**). Our objective of study was to understand the operative mechanism(s) and conditional requirements for iterative deamination chemistry. We envisioned a reductive Ni-catalyzed process could permit the *in situ* methylation of tertiary amine intermediates.[13c] In this instance, R^1 and R^2 are viewed as transferable carbon-based electrophiles and Y is representative of a non-transferrable substituent. We posited that iterative steps, including amine methylation by a hypothetical reagent, MeX (*steps i* and *iii*), and Ni-catalyzed C–N cleavage of the resultant ammonium salt intermediates **A** and **C** (*steps ii* and *iv*), could produce a Ni-III intermediate **D**, bearing a combination of the transferrable groups, R^1 and R^2. A stoichiometric reductant, such as Mn, would regulate the oxidation state of key Ni-intermediates.[19] Reductive elimination (*step iv*) from **D** ($L_nNiR^1R^2X$) or the symmetrically substituted variants **D'** ($L_nNiR^1R^1X$ or $L_nNiR^2R^2X$, *not depicted*) would provide cross- and dimeric products respectively—with unknown selectivity.[20,21] The impact of generated radical intermediates and liberated tertiary amines on Ni-catalyzed steps, as well as the potential disruption of beneficial Ni–ligand interactions, were also unknown. The discovery of a Ni-compatible methylation reagent (MeX), with chemoselectivity for tertiary amine intermediates, would render this multi-step proposal achievable in a one-pot fashion. Overall, the transformation could be described as a reductive deamination wherein two C–N bonds are cleaved and one C–C bond formed.

The advent of cross-electrophile coupling chemistry has indeed inspired the development of related Ni-catalyzed transformations that involve concurrent C–O/C–X bond cleavages (**Figure 2a**).[20,21,22] Cao and Shi report a dual C–O cleavage transform using a Ni-catalyst in combination with a stoichiometric reductant (*e.g.*, Zn) and bis(pinacolato)diboron (B_2pin_2) to affect iterative benzalkyl C–O bond cleavages.[22b] The reaction converts dibenzalkylethers into cross- and dimeric- 1,2-diarylethane products with net excision of oxygen atom. To the best of our knowledge, the analogous deaminative transform of a dibenzalkyl tertiary amine is unknown.[5,23]

For our study of iterative benzalkyl group transfers from nitrogen, we were encouraged by a report from the Martin group.[13c] They concluded that the reductive carboxylation of benzalkyl trimethylammonium salts proceeded via a Ni-catalyzed benzylic C–N bond cleavage event (**Figure 2b**). By using an atmosphere of CO_2, and Mn as a stoichiometric reductant, only benzalkyl carboxylic acids were obtained. Homodimeric products (*e.g.*, 1,2-diarylethanes) were not observed. We reasoned that similar conditions, performed under an inert atmosphere, would permit C–C coupling events (homodimerization). In addition, the electrochemical homodimerization of benzalkyl trimethylammonium salts provides fundamental reactivity precedent for C–N cleavage and C–C bond forming events that are proposed to occur via radical homocoupling.[24,25]

We hypothesized that benzalkyl trimethylammonium salts could be efficiently dimerized under reductive Ni-catalysis conditions. Until recently,[13f] Ni-catalyzed reductive coupling reactions of benzalkyl trimethylammonium salts with electrophiles other than CO_2 were unknown.[13c] During the course of our investigation, Shu and coworkers demonstrated the use of benzalkyl trimethylammonium salts as effective electrophilic partners for C–N/C–O cross-electrophile coupling with alkenyl and aryl acetates.[13f] Notably, dimeric products that

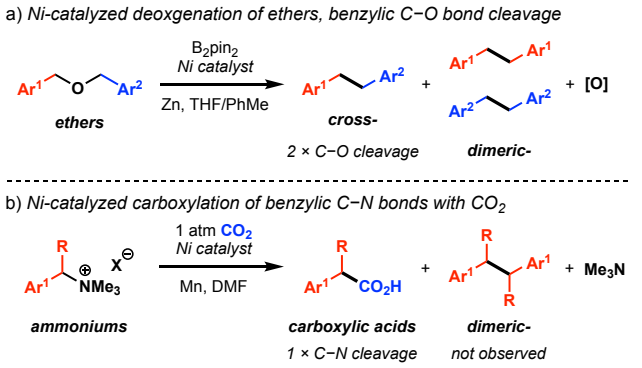


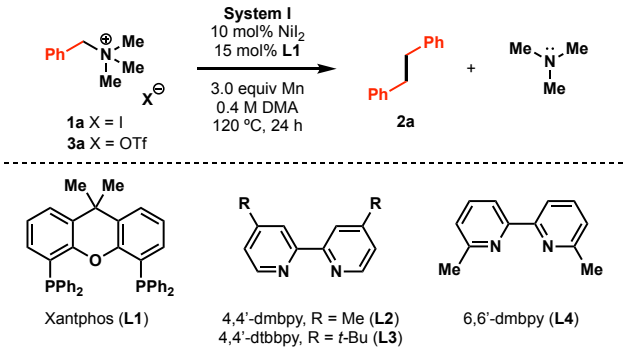
Figure 2. Ni-catalyzed cleavage of benzylic C–O and C–N bonds.

result from the homocoupling of benzalkyl trimethylammonium salts are reported. An improved understanding of such homodimerization events could be applied for the discovery of a method wherein a tertiary amine could serve to template the construction of Csp^3–Csp^3 bonds (**Scheme 1b**). Herein, we disclose results that detail the discovery of a method for iterative benzalkyl group transfer from a nitrogen atom center, enabling the formation of cross- and dimeric- 1,2-diarylethane products.

2. RESULTS AND DISCUSSION

2.1. Development of conditions for the reductive dimerization of benzalkylammonium salts. We began our studies with the systematic examination of conditions for the reductive dimerization of benzalkyl ammonium salts (**Table 1**). Optimization efforts found the reaction of benzyltrimethylammonium iodide (**1a**) with NiI_2 (10 mol%), Xantphos (**L1**, 15 mol%),[26] and Mn (3.0 equiv) in *N*,*N*-dimethylacetamide (DMA, 0.4 M) at 120 °C for 24 h to provide 1,2-diphenylethane (**2a**) in 65% isolated yield (entry 1, 'System I'). The use of Zn as an alternative co-reductant (entry 2), other Ni^{II} sources (entries 3 and 4), or dimethylformamide (DMF) in place of DMA (entry 5) were all found to result in a lower yield of **2a**. Furthermore, the use of excess ligand (**L1**, entry 6) had a deleterious effect on the yield. A representative ligand screen **L2**–**L4** (entries 7-9) highlights a preference for bidentate ligands and demonstrates the efficiency of Xantphos (**L1**, entry 1) for this transformation.[26] We found the use of 1,10-phenanthroline-based ligands to be less effective[13c] (for a complete ligand screen, see **Table S1**). Consistent with related benzalkyl C–N bond cleavage methods, this reaction proceeds without ligand (entry 10), albeit with diminished efficiency.[9e] Control experiments demonstrate the crucial role of Ni (entry 11 and 12) and Mn (entry 13). Intriguingly, the addition of (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl (TEMPO, entry 14) resulted in a slight decrease in yield albeit with no detectable TEMPO adducts (**Table 1**).[13c,27] Next, we examined the impact of tertiary amine additives on catalysis efficiency. Although the presumed reaction byproduct, trimethylamine (b.p. 2.9 °C), can be tentatively identified by its characteristic fishy odor during reaction workup, its low boiling point precludes facile quantitative analysis. Control studies found that stoichiometric addition of triethylamine (1 equiv, b.p. 89 °C, entry 15) or dimethylbenzylamine (1 equiv, b.p. 180 °C, entry 16) resulted in slightly diminished yields. This suggests that liberated tertiary amines would be tolerated in reactions that require iterative methylation and C–N bond cleavage processes. During efforts to address the mechanistic inquiry of benzyl iodide intermediates that may be formed *in situ*, we identified an alternatively effective, iodide-free process. Here, we define 'System II' (entry 17), as the reaction of benzyltrimethylammonium triflate (**3a**) with $Ni(OTf)_2$ (10 mol%), Xantphos (**L1**, 15 mol%), and Mn (3.0 equiv) in DMA (0.4 M) at 120 °C for 24 h to provide homodimer **2a** in 69% yield. System II-type conditions might find application in settings wherein benzylic halide intermediates are detrimental to product outcome and selectivity. Indeed, iodide introduced with the Ni-source, **3a** with NiI_2 (10 mol%, entry 18), or, with the substrate, **1a** with $Ni(OTf)_2$ (10 mol%, entry 19) proceeds with slightly diminished yields.

Table 1. Optimization of reaction conditions for the Ni-catalyzed reductive cleavage of benzylic C–N bonds and control experiments.



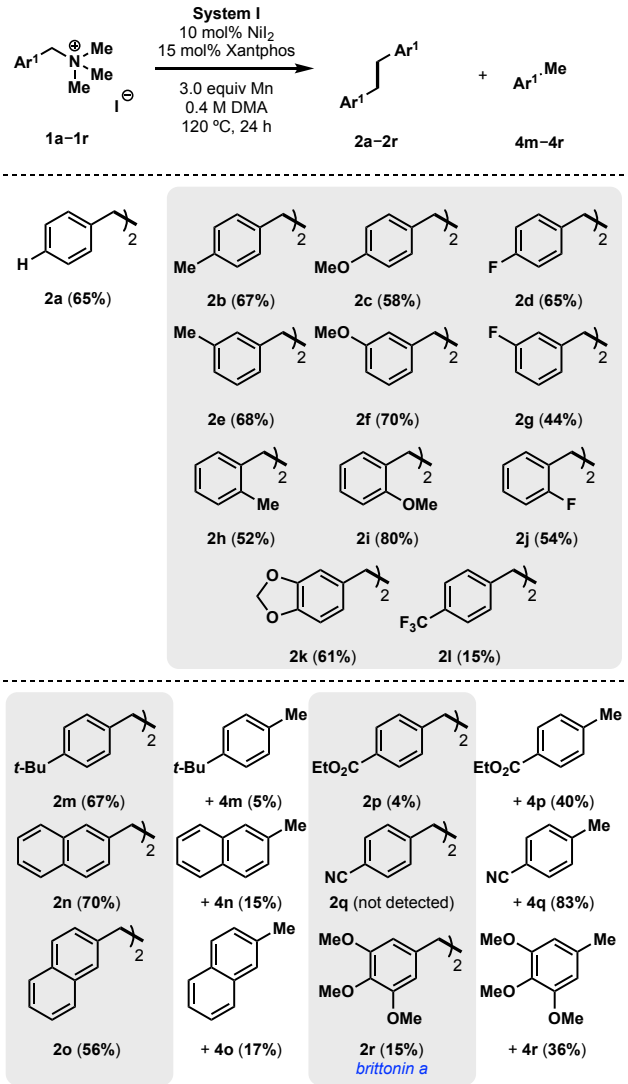
entry	deviation from standard conditions	2a (%)[a]
1	none	65
2	Zn instead of Mn	47
3	$NiBr_2$ (10 mol%)	33
4	$NiBr_2$(glyme) (10 mol%)	50
5	DMF as solvent	40
6	**L1** (30 mol%)	40
7	**L2** as ligand	42
8	**L3** as ligand	57
9	**L4** as ligand	46
10	no ligand	19
11	no NiI_2	trace
12	no NiI_2, no ligand	trace
13	no Mn	trace
14	TEMPO (1 equiv)	54
15	triethylamine (1 equiv)	48
16	dimethylbenzylamine (1 equiv)	60
17	**3a** (X = OTf), $Ni(OTf)_2$ (10 mol%) (**System II**)	69[b]
18	**3a** (X = OTf)	55
19	$Ni(OTf)_2$ (10 mol%)	60

[a]Reaction conditions: **1a** or **3a** (1.34 mmol), NiI_2 (10 mol%), Xantphos (L1) (15 mol%), Mn (3 equiv, 4.02 mmol), DMA (0.4 M) at 120 °C for 24 h; yields of isolated **2a** are provided as an average of two independent runs. [b]Yield of isolated **2a** provided as an average of four independent runs.

2.2. Reductive deaminative dimerization scope and limitations. With optimized conditions (System I), we evaluated the scope of the Ni-catalyzed reductive dimerization of benzalkyl trimethylammonium iodides (**Table 2**). A representative examination of benzalkyl ammonium iodides (**1a**–**1l**) found dimeric products (**2a**–**2l**) as the sole observable reaction products, isolable in 58% average yield (*12 examples*, **Table 2**)). Interestingly, *ortho*-substitution is tolerated, with the *ortho*-methoxy variant (**1i**) providing dimer (**2i**) with improved isolated yield relative to substrates bearing and *ortho*-methyl and *ortho*-fluoro substituent (**1h, 1j**). This is suggestive of a beneficial substrate (**1i**) Ni-chelation in C–N bond cleavage and/or C–C bond forming events.[13c]

Certain substrates (**1m**–**1r**) undergo efficient Ni-catalyzed benzylic C–N bond cleavage, yet dimerization events to access products **2m**–**2r** appear to compete with a reduction pathway (**4m**–**4r**). Extended π systems (**1n**, **1o**) permit access to dimers (**2n**, **2o**) as major products alongside reduced derivatives (**4n**, **4o**) as minor products. Electron-deficient substrates (**1p**, **1q**) favor reduction products almost exclusively (**4p**, **4q**), a result that may be reflective of the difficulty to affect their dimerization by reductive elimination. An overtly electron-rich substrate (**1r**) provided access to brittonin a (**2r**) alongside reduction product **4r**. Overall, these results (*17 examples*, 54% average yield) suggest that the developed procedure is a general method for benzylic C–N bond cleavage with successive C–C bond formation.

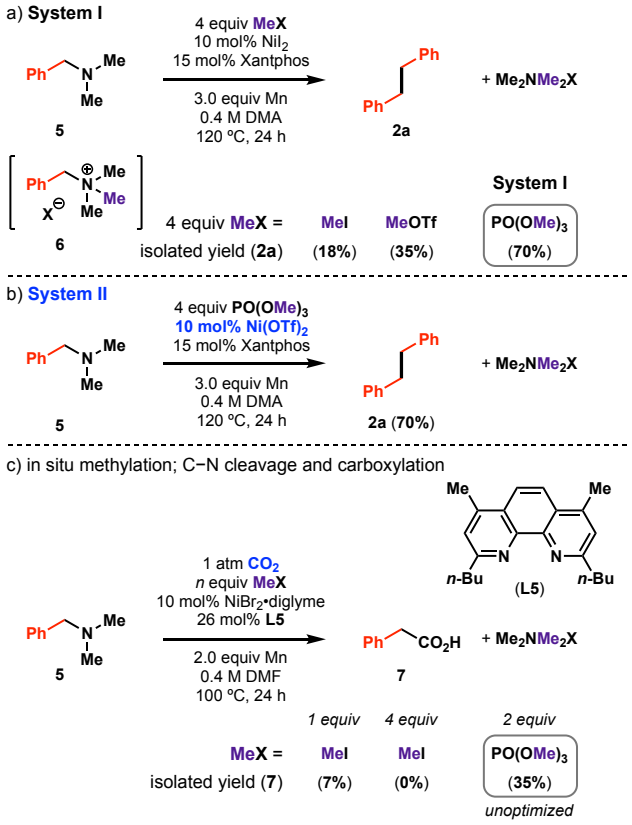
Table 2. An examination of Ni-catalyzed benzylic C–N bond cleavage and the homodimerization reactivity of ammonium substrates.



[a]Reaction conditions: **1a–1r** (1.34 mmol), NiI_2 (10 mol%), Xantphos (15 mol%), Mn (3 equiv, 4.02 mmol), DMA (0.4 M) at 120 °C for 24 h; yields of isolated products (**2a**–**2r**) and (**4m** –**4r**) are provided as an average of two independent runs.

2.3. Discovery of a Ni-compatible reagent for the *in situ* methylation of amines. Due to our familiarity with the reactivity of benzalkyl trimethylammonium salts (**1a**, **3a**), we studied the one-pot conversion of *N,N*-dimethylbenzylamine (**5**) into 1,2-diphenylethane (**2a**) (**Scheme 1**). For this, we examined a series of methylation reagents (MeI, MeOTf, $PO(OMe)_3$) in their ability to serve as Ni-compatible *in situ* methylators for the conversion of **5** into ammonium salts (confer **6**, **Scheme 1**).[13c,28] The choice of trimethylphosphate ($PO(OMe)_3$) was inspired by a report from Hartwig and co-workers that described the slow generation of MeI from the *in situ* reaction of LiI with $PO(OMe)_3$.[29] Accordingly, we wondered if $PO(OMe)_3$ could be used as an electrophile for *in situ* amine alkylation. Although $PO(OMe)_3$ is known to affect the controlled alkylation of anilines,[28] it was unclear if this electrophile would undergo deleterious reactions (*e.g.*, oxidative addition) at Ni, thereby precluding its desired utility.

Scheme 1. Discovery of reaction conditions for the in situ methylation and Ni-catalyzed cleavage of benzylic C–N bonds from tertiary amines.



[a]Yields of isolated products (**2a**) and (**7**) are provided as an average of two independent runs.

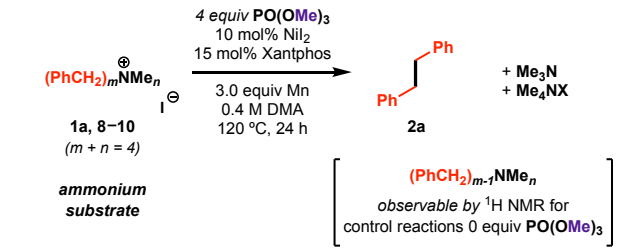
We hypothesized two possible productive scenarios that could be operative: (1) the combination of iodide, from NiI_2, and $PO(OMe)_3$ in DMA would produce low concentrations of MeI, and, MeI would react preferentially with **5** to form a Ni-reactive ammonium salt intermediate (**6**), or, (2) $PO(OMe)_3$ reacts directly with **5** to form a Ni-reactive ammonium salt intermediate (**6**). We tested these hypotheses by the comparison of 'System I' and 'System II' type conditions. Interestingly, System I conditions provide homodimer **2a** in 70% yield when 4 equiv of $PO(OMe)_3$ is employed, whereas the respective reactions with 4 equiv of MeI (18%) or 4 equiv of MeOTf (35%) are less effective (**Scheme 1a**). The control reaction of **5** with $PO(OMe)_3$ in DMA at 120 °C for 24 h afforded benzyltrimethylammonium dimethylphosphate salt **6** (X = $OPO(OMe)_2$) in 35% isolated yield. Only a single methyl group is transferred to the amine.[28] System II also affords homodimer **2a** in 70% yield (**Scheme 1b**). Additionally, using known catalysis conditions and $PO(OMe)_3$ as an additive (2 equiv), *N,N*-dimethylbenzylamine **5** can be converted to phenylacetic acid **7** (35%) (**Scheme 1c**). This unoptimized yield is significantly improved relative to the previously reported use of MeI (1 equiv, 7% and 4 equiv, 0%) as an *in situ* methylation reagent.[13c] Collectively, these studies suggest that **5** is methylated *in situ* by $PO(OMe)_3$ and the *in situ* formation of MeI is neither required nor beneficial for these transforms. Overall, this understanding of the reactivity of $PO(OMe)_3$ for the *in situ* methylation of tertiary amines is significant and supportive of the development of one-pot methods for Ni-

catalyzed cleavage and functionalization of benzylic C–N bonds.

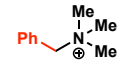
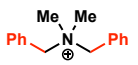
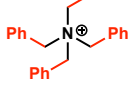
2.4. Trimethylphosphate for iterative benzalkyl transfer from ammoniums and amines. The abovementioned results support the chemoselectivity of $PO(OMe)_3$ for tertiary amine methylation in the presence of low-valent Ni-intermediates. Conversion for one benzalkyl transfer event, defined herein as 1 × methylation and 1 × C–N cleavage, occurs with 70% overall yield using either System I, or System II conditions. This efficiency suggested that iterative benzalkyl transfer chemistry could be possible. We first examined the reactivity of mono- (**1a**), di- (**8**), tri- (**9**) and tetra- (**10**) benzylammonium salts (**Table 3**). Based on our nascent understanding, we expect benzyl trialkylammonium salts (**1a**, **8**–**10**: $(PhCH_2)_mNMe_nI$, *where* $m + n = 4$), reacted under control conditions without $PO(OMe)_3$ (System I), to only transfer a single benzyl group. This benzyl group transfer event would generate the respective tertiary amine represented by the formula: $(PhCH_2)_{m-1}NMe_n$. Interestingly, singular benzyl group transfer proceeds with increasing efficiency for the series (**1a**, **8**–**9**). Substrates **1a**, **8**, and **9**, provide homodimer (**2a**) in 65%, 70% and 76% yield, respectively. The tertiary amines liberated from experiments with **8** and **9**, benzyl dimethylamine and dibenzyl methylamine, respectively, can be observed by ^{1}H NMR analysis of the crude reaction mixture and support the claim of singular benzyl transfer (*see the Supporting Information*). Attempts to prepare tetrabenzylammonium iodide were unsuccessful. We attribute this to a presumed facile nucleophilic dealkylation by the iodide counterion, as tribenzylamine is recovered from attempted alkylations with benzyl iodide. Instead, tetrabenzylammonium tosylate **10** could be prepared, however, this substrate was not productive under catalytic conditions (*see the Supporting Information*).

Table 3. An examination of iterative alkyl transfer efficiency from benzyl ammonium substrates. Support for single, double and triple benzylic C–N bond cleavage events.

a) iterative benzyl transfer from tetraalkyl ammoniums



b) theoretical and observed benzyl group transfers:[a]

		control: 0 equiv $PO(OMe)_3$ (theoretical transfers)	isolated **2a** (%)	4 equiv $PO(OMe)_3$ (theoretical transfers)	isolated **2a** (%)
1a		*1 benzyl*	65	*1 benzyl*	42
8		*1 benzyl*	70	*2 benzyls*	46 *calc.* [68%]^2
9		*1 benzyl*	76	*3 benzyls*	47 *calc.* [78%]^3
10		*1 benzyl*	ND[b]	*4 benzyls*	- -

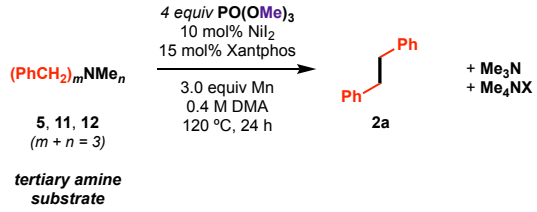
[a]Yields of isolated products (**2a**) are provided as an average of two independent runs. Yields are calculated on the basis of available benzyl groups for each substrate. For example, 1 mol of compound **8**, bearing two benzyl groups, can theoretically provide 1 mol of 1,2-diphenylethane (**2a**). For reactions run in the absence of trimethylphosphate, the generated tertiary amines can be observed quantitatively by ^{1}H NMR analysis of the crude reaction mixture. [b]Homodimer **2a** is not detected [ND] upon ^{1}H NMR analysis of the crude reaction mixture.

We next examined C–N cleavage efficiency for the series of benzyl trialkylammonium salts (**1a**, **8**–**9**) in the presence of 4 equiv of $PO(OMe)_3$ (**Table 3**). We observe a diminished yield for the conversion of **1a** into **2a** (42%). For a transformation that does not require methylation, this result suggests that excessive $PO(OMe)_3$ may exhibit a deleterious effect on catalysis. Conversely, when $PO(OMe)_3$ can be utilized, dibenzyl dimethylammonium (**8**) and tribenzyl methylammonium (**9**) salts permit double and triple benzyl transfers, to form **2a** with 46% and 47% overall efficiency, respectively. To better understand reactivity trends of benzyl group transfer across varied substrates, we define the efficiency of a single transfer event as the overall yield of three combined events [1 × methylation, 1 × C–N bond cleavage, 1 × C–C bond formation]$^{\#\ \text{of iterations}}$. From this definition, iterative yields can be calculated for double, $[68\%]^2 = 46\%$, and triple, $[78\%]^3 = 47\%$, benzyl transfer reactions. Again, the trend of increasing group transfer efficiency appears to track with the increasing electron density for the initial ammonium substrate (**Table 3**: double from **8**, [68%]; triple from **9**, [78%]). These results are significant and demonstrate the efficiency of optimized conditions for iterative benzyl group transfers. For example, no fewer than six discrete events must take place during the conversion of tribenzyl methylammonium **9** into homodimer **2a**: 2 × methylations, 3 × C–N bond cleavages, and concomitant C–C bond formation. No benzyl tertiary amine byproducts are observable in all reactions conducted with 4 equiv $PO(OMe)_3$. It is also noteworthy that these iterative transfers are achievable without an increase in catalyst, ligand or reductant loading.

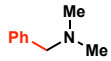
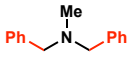
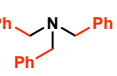
The efficiency of the abovementioned results suggested that intermediary tertiary amines (**5**, **11**, **12**) methylated *in situ* by $PO(OMe)_3$ under catalysis conditions would also exhibit benzalkyl group transfer chemistry (**Table 4**). *Control experiments demonstrate that benzyl transfer will not occur without methylation (i.e., benzyl transfer is not possible using System I conditions). In situ* methylation with $PO(OMe)_3$ would eliminate the need for the preparation and isolation of intermediary ammonium salts. As anticipated from experiments with **5** (**Scheme 1**, 70% of **2a**), tertiary amines **11** and **12** also reacted under the same catalytic conditions with 4 equiv of $PO(OMe)_3$ to permit two and three benzyl transfers, calculated as $[60\%]^2 = 36\%$ and $[69\%]^3 = 33\%$ of homodimer **2a**, respectively. Here the trend of increasing efficiency for the series (**11**, **12**) is also observed by comparison of iterative yields, double, [60%] and triple, [69%], respectively. The decreasing overall yields for the series (**5**, **11**, **12**) are attributed to the difficulty of the initial methylation event (*see the Supporting Information*). Notwithstanding the inefficiency of the first methylation, the one-pot conversion of tribenzylamine **12** with $PO(OMe)_3$ into homodimer **2a** must involve no fewer than seven discrete events, including, 3 × methylations, 3 × C–N cleavages, as well as concomitant C–C bond formation. A stepwise breakdown indicates that at least seven events must proceed with an overall efficiency per event of $[85\%]^7 = 33\%$.

Table 4. An examination of iterative alkyl transfer efficiency from benzyl amine substrates. Support for single, double and triple benzylic C–N bond cleavage events.

a) iterative benzyl transfer from tertiary amines



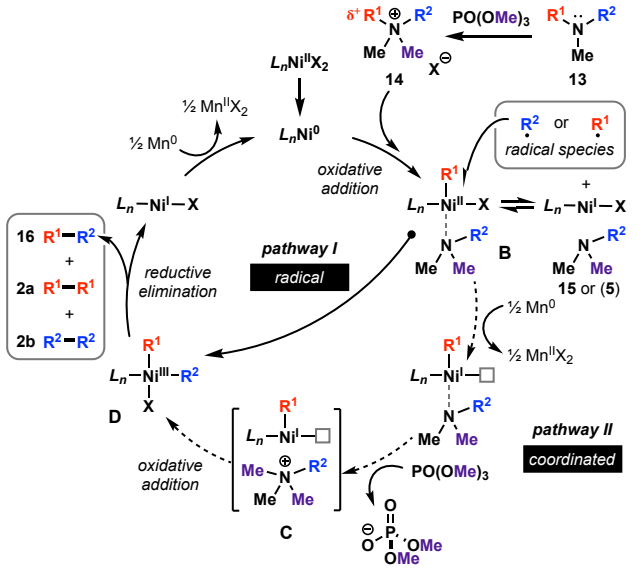
b) theoretical and observed benzyl group transfers:[a]

		control: 0 equiv PO(OMe)$_3$ (theoretical transfers)	4 equiv PO(OMe)$_3$ (theoretical transfers)	isolated **2a** (%)
5		*0 benzyls*	*1 benzyl*	70
11		*0 benzyls*	*2 benzyls*	36 *calc.* [60%][2]
12		*0 benzyls*	*3 benzyls*	33[b] *calc.* [69%][3]

[a]Yields of isolated products (**2a**) are provided as an average of two independent runs. [b]Reaction performed with excess PO(OMe)$_3$ (8 equiv, 120 °C, 5 d.

2.5. Proposed reaction pathways and a mechanistic study: reductive deamination of an unsymmetrical tertiary amine. Next we studied this reductive deamination process in the context of an unsymmetrical tertiary amine substrate (**13**), bearing R^1 = benzyl and R^2 = *para*-methylbenzyl substituents (**Scheme 2**). We reasoned that the reactivity of this substrate, as measured by product ratios, compared to a series of related crossover experiments would provide mechanistic insight. As proposed, we anticipated the *in situ* methylation of a benzalkyl

Scheme 2. Proposed pathways for the *in situ* methylation of tertiary amines; Ni-catalyzed C–N bond cleavage and C*sp*^{3}–C*sp*^{3} bond formation.

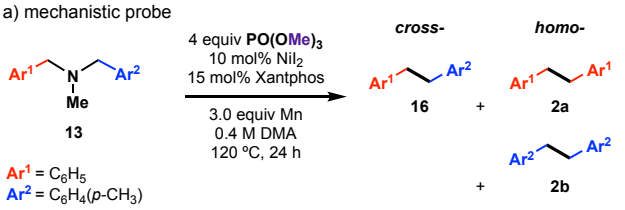


tertiary amine **13**, followed by indiscriminate C–N bond cleavage (R^1 or R^2, R^1 depicted as first cleavage) from ammonium **14** would generate a benzalkylated Ni-intermediate (**B**). Intermediate **B** could proceed along two pathways proposed as follows: (1) the disproportionation of Ni-intermediate **B** would generate a low-valent Ni intermediate, a dissociated tertiary amine (**15** *or* **5**) and a mixture of benzylic radical species; with benzylic radical intermediates ultimately leading to a mixture of cross, **16**, and dimeric products, **2a** and **2b** (**pathway I**), or alternatively; (2) significant tertiary amine coordination during reduction and methylation events could provide proposed intermediate **C** along an amine-coordinated path (**pathway II**). The generation of an ammonium in proximity to a low-valent Ni-intermediate (**C**) could enable cross-selective oxidative addition to access intermediate **D**. The overall conversion of **B** to **D** with selectivity for cross-product (**16**) formation would support a molecule-to-molecule transformation consistent with **pathway II**.

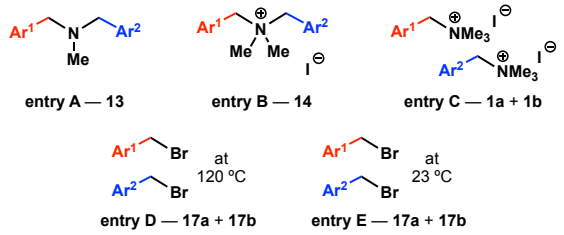
An examination of reaction mechanism by evaluation of a non-symmetric amine (**13**, entry A) and relevant crossover experiments (entries B–F) is presented in **Table 5**. As a hypothetical reference point, a statistical distribution of **16**:**2a**:**2b**, 0.5:0.25:0.25, is provided as part of **Table 5** (entry F). All product distributions (**16**:**2a**:**2b**) for these experiments are normalized ratios (*see the Supporting Information*).

Table 5. An examination of reaction mechanism by evaluation of an unsymmetrical tertiary amine substrate

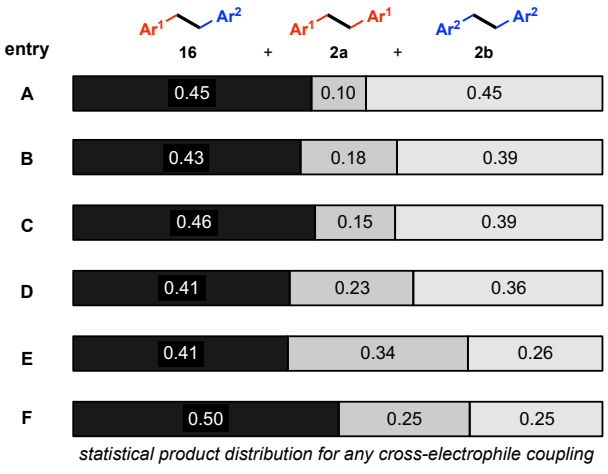
a) mechanistic probe



b) evaluated substrates:



c) normalized product distributions:



Using optimal conditions, tertiary amine **13** with 4 equiv $PO(OMe)_3$ afforded cross-product and dimeric products (**16**:**2a:2b**) with a 0.45:0.10:0.45 ratio (**Table 5**, entry A). The pre-methylated variant, ammonium iodide (**14**), afforded a similar product distribution 0.45:0.18:0.39 (entry B), albeit with improved overall conversion. The comparison of these product distributions (entry A and entry B) suggests the tertiary amine (**13**) and the ammonium substrate (**14**) operate along a similar mechanistic pathway. This is consistent with our understanding of *in situ* methylation and the compatibility of this step with concurrent C–N bond cleavage events. Furthermore, the crossover experiment of two different ammonium iodide salts (0.5 equiv **1a**, 0.5 equiv **1b**) produced nearly the same ratio of products, 0.46:0.15:0.39 (entry C). This result suggests that amine coordination events (**Scheme 2**, confer **B → C**, **pathway II**) do not augment cross-product (**16**) formation selectivity. However, there is a marked selectivity observed for the homodimeric products (**2a**:**2b**, ~1:3). We attribute this outcome to the relative stability of the *para*-methyl benzyl radical leading to the favorable formation of homodimer **2b**.[30] Additional control crossover experiments with comparable organohalide substrates, benzyl bromide (**17a**) and para-methyl benzyl bromide (**17b**) were also informative. Using the conditions optimized for ammonium substrates (120 °C, $PO(OMe)_3$ excluded), 0.5 equiv **17a** with 0.5 equiv **17b** provided products in a 0.41:0.23:0.36 ratio (entry D). The same reaction run at room temperature afforded a largely statistical product distribution consistent with benzalkyl radical coupling (0.41:0.34:0.26, entry E).[31] Again, the higher temperature experiment supports the dependence of product outcome on the stability of benzylic radical intermediates.[32] Overall, these deaminative coupling (entries A–C) and benzalkyl bromide crossover experiments (entries D–E) support the Ni-catalyzed coupling of benzylic radical intermediates (**Scheme 2**).[20,26c,33]

Our product distributions are also in agreement with the related deoxygenative transforms reported by the Shi group.[22b] In this related transform, dual C–O bond cleavage events must proceed in a stepwise fashion. The dual C–N bond cleavage results presented here are consistent in this aspect. Likewise, the key reagents, B_2pin_2 for C–O bond activation, and $PO(OMe)_3$ for C–N bond activation, are compatible with reductive Ni-catalysis. The statistical distribution of cross- and dimeric products in both transforms support a mechanism involving Ni-benzalkyl intermediates.[22b,24,26c,27] Recent studies from the Shu laboratory support a similar convergence of benzylic radical intermediates for the Ni-catalyzed cleavage of ammonium salts (C–N bond) coupled with aryl tosylates (C–O bond) under reductive conditions.[13f]

2.6. Proposed mechanism. Based upon our findings and related transforms,[13c,13f,20a,26c] we propose a mechanism for the deamination of tertiary amines consistent with **pathway I** (**Scheme 2**). First, the *in situ* methylation of a tertiary amine (**13**) forms an activated ammonium intermediate (**14**). Oxidative addition affords benzalkylated Ni-intermediate **B**. The generation and interception of benzylic radical species by this intermediate (**B**) leads to dibenzalkylated intermediates, **D** ($L_nNiR^1R^2X$) and **D'** ($L_nNiR^1R^1X$ or $L_nNiR^2R^2X$, *not shown*). Reductive elimination affords both cross, **16**, and dimeric products, **2a** and **2b**, in largely statistical distributions.[22b,26c] Finally, reduction of the resultant Ni(I) intermediate by Mn serves to regenerate Ni(0). Intermediary tertiary amines (*e.g.*, **5**, **15**) are methylated by $PO(OMe)_3$ and processed by Ni-catalyzed C–N bond cleavage events. Although we cannot exclude events proposed along coordinated **pathway II** (**Scheme 2**, reduction; *in situ* tertiary amine methylation), we do not observe product distributions consistent with a molecule-to-molecule transformation (*i.e.* the direct conversion of **13 → 16** at a single Ni-center).

3. CONCLUSION

In summary, we have demonstrated a method for Ni-catalyzed iterative alkyl transfer from tertiary amines and ammoniums. We reveal the utility of trimethylphosphate, $PO(OMe)_3$, as a Ni-compatible reagent for achieving *in situ* methylation of tertiary amines. In combination with Ni-catalysis, this inexpensive reagent permits iterative methylation, Csp^3–N bond cleavage and Csp^3–Csp^3 bond forming events. We show the use of this method for the homodimerization or carboxylation of benzalkyl dimethylamines and benzalkyl trimethylammonium salts. We anticipate the adoption of $PO(OMe)_3$ as a Ni-compatible methylation reagent to streamline related reactions that involve benzalkyl C–N bond cleavage of ammonium salt intermediates.[9] An understanding of dual C–N bond cleavage permits the deamination of dibenzalkyl methylamines to access 1,2-diarylethane scaffolds. Up to three benzyl group transfers are possible from a single tertiary amine substrate. A preliminary survey of deaminative, as well as related crossover experiments, support the involvement of benzylic radical intermediates consistent with proposed **pathway I**. Future studies will evaluate conditions to favor tertiary amine coordination events and/or ammonium ion pairing[18] with the Ni-catalyst in an effort to promote cross-selectivity in these deaminative transforms.

4. EXPERIMENTAL SECTION

General information. Solvents and reagents were purchased from commercial distributors and used as received. It is worthy to note that *N*,*N*-dimethylacetamide (DMA) purchased from Merck Millipore was superior. Manganese powder -325 mesh was purchased from Sigma Aldrich. All Ni-catalyzed reactions were performed under a positive pressure of N_2 in a round bottom flask equipped with a reflux condenser. ^1H and ^{13}C NMR spectra were obtained either on a Varian 400 or 500 MHz Unity INOVA spectrometer. All ^1H NMR spectra are reported in parts per million (ppm) relative to residual $CHCl_3$ (7.26 ppm) or H_2O (4.79 ppm). Coupling constants, *J,* are reported in Hertz (Hz). All ^{13}C NMR spectra are reported in ppm relative to residual $CHCl_3$ (77.2 ppm). High resolution mass spectra were recorded at the Mass Spectrometry Facility in the Department of Chemistry at the University of Utah on a Finnigan MAT® 95 double focusing high resolution mass spectrometer. Low resolution mass spectra were recorded on Advion expression compact mass spectrometer (CMS). Column chromatography was carried out using 230-400 mesh silica gel purchased from Silicycle and used as received. Melting points are reported in degrees Celsius (°C) with a Mel-Temp II melting point apparatus. *N*,*N*-dimethylbenzylamines were prepared either from the corresponding benzyl amines using Eschweiler–Clarke conditions[34] or via alkylation of dimethylamine with the corresponding benzyl halides.[35,36] The amines were used without purification.

General procedure for the preparation of mono-benzyl ammonium iodides. *Synthesis of **1a-1r**.* Dimethylbenzylamine (1 equiv.) was dissolved in ethyl acetate (1.0 M). Methyl iodide (3 equiv.) was added dropwise at room temperature, and the entire mixture stirred at room temperature for 1 h. The resultant precipitate was filtered, and the filtrate washed with ethyl acetate (10 mL × 4) to afford the corresponding salt. If necessary, the benzyl trimethylammonium iodide salt was recrystallized from a 4:1 mixture of 2-propanol:toluene.

***N,N,N*-trimethyl-1-phenylmethanaminium iodide (1a)**.[37] Reaction performed with 16 mmol of amine in 16 mL ethyl acetate. **1a** was recrystallized to afford white needle-like crystals (4.2 g, 96%); mp: 176–177 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, J = 7.9 Hz, 2H), 7.49 – 7.40 (m, 3H), 5.05 (s, 2H), 3.40 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz, D_2O): δ 132.9, 130.9, 129.3, 127.4, 69.6, 52.6; LRMS (ESI$^+$): *Calcd.* for $C_{10}H_{16}N$ [M-I]: 150.13, found 150.23.

***N,N,N*-trimethyl-1-(p-tolyl)methanaminium iodide (1b)**.[37] Reaction performed with 7.1 mmol of amine in 7 mL ethyl acetate. **1b** was isolated as a white solid (1.7 g, 80%) and recrystallized; mp: 208–210 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, J = 7.7 Hz, 2H), 7.18 (d, J = 7.5 Hz, 2H), 4.95 (s, 2H), 3.37 (s, 9H), 2.36 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 141.1, 133.0, 129.9, 124.2, 68.6, 52.7, 21.3; LRMS (ESI$^+$): *Calcd.* for $C_{11}H_{18}N$ [M-I]: 164.14, found 164.23.

1-(4-methoxyphenyl)-*N,N,N*-trimethylmethanaminium iodide (1c).[37] Reaction performed with 16 mmol of amine in 16 mL ethyl acetate. **1c** was isolated as a white solid (3.7 g, 77%); mp: 157–158 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, J = 8.5 Hz, 2H), 6.93 (d, J = 8.5, 2H), 4.96 (s, 2H), 3.81 (s, 3H), 3.35 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.4, 134.5, 119.1, 114.6, 68.3, 55.5, 52.5; LRMS (ESI$^+$): *Calcd.* for $C_{11}H_{18}NO$ [M-I]: 180.14, found 180.25.

1-(4-fluorophenyl)-*N,N,N*-trimethylmethanaminium iodide (1d).[13c] Reaction performed with 16 mmol of amine in 16 mL ethyl acetate. **1d** was isolated as a white solid (4.6 g, 95%); mp: 238–239 °C; ^{1}H NMR (500 MHz, D_2O): δ 7.46 (dd, J = 8.7, 5.6 Hz, 1H), 7.16 (t, J = 8.7 Hz, 2H), 4.37 (s, 2H), 2.98 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz, D_2O) 163.9 (d, J_{CF} = 248.3 Hz), 134.9 (d, J_{CF} = 9.1 Hz), 123.4, 116.1 (d, J_{CF} = 22.0 Hz), 68.7, 52.2; LRMS (ESI$^+$): *Calcd.* for $C_{10}H_{15}FN$ [M-I]: 168.12, found 168.08.

***N,N,N*-trimethyl-1-(m-tolyl)methanaminium iodide (1e)**.[13c] Reaction performed with 5.3 mmol of amine in 6 mL ethyl acetate. **1e** was isolated as a white solid (1.1 g, 71%); mp: 200–201 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51 – 7.40 (m, 2H), 7.33 – 7.26 (m, 2H), 4.98 (s, 2H), 3.42 (s, 9H), 2.36 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 139.2, 133.5, 131.7, 130.2, 129.2, 127.1, 70.0, 52.9, 21.4; LRMS (ESI$^+$): *Calcd.* for $C_{11}H_{18}N$ [M-I]: 164.14, found: 164.07.

1-(3-methoxyphenyl)-*N,N,N*-trimethylmethanaminium iodide (1f).[13c] Reaction performed with 16 mmol of amine in 16 mL ethyl acetate. **1f** was obtained as a white solid (3.4 g, 70%); mp: 140–141 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 – 7.32 (m, 1H), 7.30 – 7.29 (m, 1H), 7.20 (dt, J = 7.6, 1.3 Hz, 1H), 7.01 (dt, J = 8.4, 1.4 Hz, 1H), 5.01 (s, 2H), 3.83 (s, 3H), 3.42 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 160.0, 130.3, 128.4, 125.1, 118.5, 116.7, 68.8, 55.9, 53.1; LRMS (ESI$^+$): *Calcd.* for $C_{11}H_{18}NO$ [M-I]: 180.14, found 180.12.

1-(3-fluorophenyl)-*N,N,N*-trimethylmethanaminium iodide (1g). Reaction performed with 9.3 mmol of amine in 10 mL ethyl acetate. **1g** was isolated as a white solid (1.7 g, 62%) and recrystallized; mp: 184–185 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (d, J = 7.8 Hz, 1H), 7.49 – 7.38 (m, 2H), 7.21 – 7.17 (m, 1H), 5.14 (s, 2H), 3.42 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.9 (d, J_{CF} = 250.7 Hz), 135.4 (d, J_{CF} = 2.1 Hz), 133.7 (d, J_{CF} = 8.6 Hz), 125.5 (d, J_{CF} = 3.8 Hz), 116.4 (d, J_{CF} = 21.9 Hz), 114.8 (d, J_{CF} = 13.8 Hz), 62.7, 53.3; HRMS (ESI$^+$): *Calcd.* for $C_{10}H_{15}FN$ [M-I]: 168.1189, found 168.1189.

***N,N,N*-trimethyl-1-(*m*-tolyl)methanaminium iodide (1h)**.[37] Reaction performed with 16 mmol of amine in 16 mL ethyl acetate. **1h** was isolated as a white solid (2.7 g, 89%); mp: 210–212 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.64 (d, J = 7.6 Hz, 1H), 7.35 (t, J = 7.5 Hz, 1H), 7.29 – 7.21 (m, 2H), 4.98 (s, 2H), 3.44 (s, 9H), 2.53 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 139.9, 134.6, 132.0, 131.0, 126.6, 125.76, 66.5, 53.1, 21.2; LRMS (ESI$^+$): *Calcd.* for $C_{11}H_{18}N$ [M-I]: 164.14, found 164.09.

1-(3-methoxyphenyl)-*N,N,N*-trimethylmethanaminium iodide (1i).[13c] Reaction performed with 6.0 mmol of amine in 6 mL ethyl acetate. **1i** was isolated as a white solid (1.5 g, 81%); mp: 151–152 °C; ^{1}H NMR (500 MHz, D_2O): δ 7.43 (t, J = 8.3 Hz, 1H), 7.32 (d, J = 7.6 Hz, 1H), 7.03 (d, J = 8.5 Hz, 1H), 6.97 (t, J = 7.5 Hz, 1H), 4.34 (s, 2H), 3.75 (s, 3H), 2.95 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz, D_2O): δ 158.8, 134.8, 132.9, 120.8, 115.6, 112.1, 63.8, 55.5, 52.6; LRMS (ESI$^+$): *Calcd.* for $C_{11}H_{18}NO$ [M-I]: 180.14, found 180.13.

1-(2-fluorophenyl)-*N,N,N*-trimethylmethanaminium iodide (1j). Reaction performed with 6.5 mmol of amine in 7 mL ethyl acetate. **1j** was isolated as a white solid (1.8 g, 94%) and recrystallized; mp: 174–175 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.92 (td, J = 7.4, 1.8 Hz, 1H), 7.52 (d, J = 7.3 Hz, 1H), 7.34 – 7.27 (m, 1H), 7.19 (t, J = 9.1 Hz, 1H), 5.01 (s, 2H), 3.47 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz, D_2O): δ 162.4 (d, J_{CF} = 244.5 Hz), 131.0 (d, J_{CF} = 8.4 Hz), 128.82, 119.5 (d, J_{CF} = 22.2 Hz), 117.8 (d, J_{CF} = 20.9 Hz), 68.7, 52.6; HRMS (ESI$^+$): *Calcd.* for $C_{10}H_{15}FN$ [M-I]: 168.1189, found 168.1188.

1-(benzo[*d*][1,3]dioxol-5-yl)-*N,N,N*-trimethylmethanaminium iodide (1k).[13c] Reaction performed with 9.5 mmol of amine in 10 mL ethyl acetate. **1k** was isolated as a white solid (1.5 g, 50%); mp: 221–222 °C; ^{1}H NMR (400 MHz, D_2O): δ 6.92 – 6.85 (m, 2H), 5.91 (s, 2H), 4.26 (s, 2H), 2.93 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz, D_2O): δ 149.2, 147.7, 127.5, 120.7, 112.4, 108.8, 101.8, 69.4, 52.2; LRMS (ESI$^+$): *Calcd.* for $C_{11}H_{16}NO_2$ [M-I]: 194.12, found 194.21.

***N,N,N*-trimethyl-1-(4-(trifluoromethyl)phenyl)methanaminium iodide (1l)**. Reaction performed with 20 mmol of amine in 20 mL ethyl acetate. **1l** was isolated as a white solid (6.5 g, 96%); mp: 175–176 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.93 (d, J = 7.9 Hz, 2H), 7.71 (d, J = 7.9 Hz, 2H), 5.30 (s, 2H), 3.46 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 133.8, 133.2, 131.1, 126.2, 124.5, 67.2, 53.1; HRMS (ESI$^+$): *Calcd.* for $C_{11}H_{15}F_3N$ [M-I]: 218.1157, found 218.1161.

1-(4-(*tert*-butyl)phenyl)-*N,N,N*-trimethylmethanaminium iodide (1m).[37] Reaction performed with 7.0 mmol of amine in 7 mL ethyl acetate. **1m** was isolated as a white solid (1.7 g, 73%); mp: 211–212 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, J = 8.0 Hz, 2H), 7.45 (d, J = 8.0 Hz, 2H), 4.95 (s, 2H), 3.40 (s, 9H), 1.29 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 154.3, 132.9, 126.2, 124.2, 68.6, 52.8, 34.9, 31.2; LRMS (ESI$^+$): *Calcd.* for $C_{14}H_{24}N$ [M-I]: 206.19, found 206.25.

***N,N,N*-trimethyl-1-(naphthalene-2-yl)methanaminium iodide (1n)**.[13c] Reaction performed with 17 mmol of amine in 17 mL ethyl acetate. **1n** was isolated as a pale orange solid (3.7 g, 65%); mp: 179–180 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.18 (s, 1H), 7.98 – 7.78 (m, 3H), 7.71 (dd, J = 8.4, 1.7 Hz, 1H), 7.63 – 7.43 (m, 2H), 5.26 (s, 2H), 3.46 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 133.9, 133.7, 132.8, 129.2, 129.0, 128.5, 127.9, 127.8, 127.1, 124.5, 68.8, 53.0; LRMS (ESI$^+$): *Calcd.* for $C_{14}H_{18}N$ [M-I]: 200.14, found 200.28.

***N,N,N*-trimethyl-1-(naphthalene-1-yl)methanaminium iodide (1o)**. Reaction performed with 17 mmol of amine in 17 mL ethyl acetate. **1o** was isolated as a white solid (2.9 g, 52%) and recrystallized; mp: 213–215 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.54 (d, J = 8.6 Hz, 1H), 8.14 (d, J = 8.3 Hz, 1H), 8.06 (d, J = 8.1 Hz, 1H), 7.82 (d, J = 7.1 Hz, 1H), 7.76 – 7.50 (m, 3H), 5.11 (s, 2H), 3.13 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6): δ 134.11,134.08, 133.3, 131.8, 129.5, 127.8, 126.8, 125.8, 125.0, 124.6, 64.2, 52.7; HRMS (ESI$^+$): *Calcd.* for $C_{14}H_{18}N$ [M-I]: 200.1434, found 200.1438.

1-(4-(methoxycarbonyl)phenyl)-*N,N,N*-trimethylmethammonium iodide (1p). Reaction performed with 8.6 mmol of amine in 9 mL ethyl acetate. **1p** was isolated as a white solid (2.6 g, 92%); mp: 196–197 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.09 (d, J = 7.9 Hz, 2H), 7.82 (d, J = 8.1 Hz, 2H), 5.25 (s, 2H), 3.95 (s, 3H), 3.46 (s, 4H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.0, 133.3, 132.6, 131.7, 130.3, 67.7, 53.1, 52.6; HRMS (ESI$^+$): *Calcd.* for $C_{12}H_{18}NO_2$ [M-I]: 208.1338, found 208.1339.

1-(4-cyanophenyl)-*N,N,N*-trimethylmethanaminium iodide (1q). Reaction performed with 13 mmol of amine in 13 mL ethyl acetate. **1q** was isolated as a white solid (2.86 g, 71%); mp: 232–233 °C; ^{1}H NMR (500 MHz, D_2O): δ 7.80 (d, J = 8.4 Hz, 2H), 7.62 (d, J = 8.3 Hz, 2H), 4.48 (s, 2H), 3.02 (s, 2H); $^{13}C\{^1H\}$ NMR (125 MHz, D_2O): δ 133.5, 133.1, 132.4, 118.7, 113.5, 68.5, 52.6; HRMS (ESI$^+$): *Calcd.* for $C_{11}H_{15}N_2$ [M-I]: 175.1230, found 175.1237.

(3,4,5-trimethoxyphenyl)-1-*N,N,N*-trimethylammoniun iodide (1r). Reaction performed with 3.1 mmol of amine in 3 mL ethyl acetate. **1r** was isolated as a white solid (879 mg, 77%); mp: 207–209 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.00 (s, 1H), 4.97 (s, 2H), 3.86 (s, 6H), 3.81 (s, 3H), 3.38 (s, 9H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 153.5, 139.8, 122.6, 110.6, 68.7, 60.9, 57.0, 53.0; HRMS (ESI$^+$): *Calcd.* for $C_{13}H_{22}NO_3$ [M-I]: 240.1600, found 240.1604.

General procedure for reductive homodimerization.

*Synthesis of **2a-2r***: A 25 mL oven dried round bottom flask equipped with a magnetic stir bar was evacuated and charged with catalyst NiI_2 (42 mg, 0.134 mmol) and Xantphos (115 mg, 0.2 mmol) under positive pressure of nitrogen. Degassed DMA (3.4 mL, 0.4 M) was added via a syringe and the entire mixture stirred for 5 mins at 120 °C (oil bath)

after which the solution became homogeneous and the color changed from grey to red. Manganese (219 mg, 4 mmol) and benzyl trimethylammonium salt (1.34 mmol) were then added to the mixture. The flask was then equipped with a condenser and the entire mixture stirred under nitrogen at 120 °C (oil bath) for 24 h. The mixture was cooled to room temperature and subsequently extracted with ether (20 mL × 3). The combined organic extract was washed with water (20 mL× 2), followed by brine (10 mL). The organic layer was then dried over Na_2SO_4, filtered and solvent removed under reduced pressure. The crude mixture was purified by flash column chromatography on silica gel.

1,2-Diphenylethane (**2a**).[38] Isolated as an off-white solid (79 mg, 0.43 mmol, 65%) via flash column chromatography with hexanes as the eluent; R_f = 0.56 (hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 – 7.29 (m, 4H), 7.22 – 7.20 (m, 6H), 2.91 (s, 4H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 141.8, 128.5, 128.4, 126.0, 38.0; LRMS (EI$^+$): *Calcd.* for $C_{14}H_{14}$ [M$^+$]: 182.11, found 182.20.

1,2-di-p-tolylethane (**2b**).[39] Isolated as a white solid (94 mg, 0.45 mmol, 67%) via flash column chromatography with hexanes as the eluent; R_f = 0.40 (hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09 (s, 5H), 2.86 (s, 4H), 2.32 (s, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 138.9, 135.0, 129.0, 128.3, 37.6, 21.0; LRMS (EI$^+$): *Calcd.* for $C_{16}H_{18}$ [M$^+$]: 210.14; found 210.20.

1,2-bis(4-methoxyphenyl)ethane (**2c**).[40] Isolated as a white solid (94 mg, 0.38 mmol, 58%) via flash column chromatography with a 20:1 mixture of hexanes/ethyl acetate as the eluent; R_f = 0.40 (20:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09 (d, J = 8.6 Hz, 4H), 6.83 (d, J = 8.6 Hz, 4H), 3.79 (s, 6H), 2.84 (s, 4H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 157.8, 134.0, 129.4, 113.7 55.2, 37.3; LRMS (EI$^+$): *Calcd.* for $C_{16}H_{18}O_2$ [M$^+$]: 242.13, found 242.20.

1,2-bis(4-fluorophenyl)ethane (**2d**).[39] Isolated as a white solid (92 mg, 0.42 mmol, 63%) via flash column chromatography with hexanes as the eluent; R_f = 0.37 (hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (dd, J = 8.6, 5.6 Hz, 4H), 6.98 (t, J = 8.7 Hz, 4H), 2.90 (s, 4H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.4 (d, J_{CF} = 243.6 Hz), 137.0 (d, J_{CF} = 3.1 Hz), 129.9 (d, J_{CF} = 7.7 Hz), 115.1 (d, J_{CF} = 21.0 Hz), 37.2; ^{19}F NMR (282 MHz, $CDCl_3$): δ -117.8; LRMS (EI$^+$): *Calcd.* for $C_{14}H_{12}F_2$ [M$^+$]: 218.09, found 218.20.

1,2-di-m-tolylethane (**2e**).[39] Isolated as a colorless oil (95.4 mg, 0.45 mmol, 68%) via flash column chromatography with hexanes as the eluent; R_f = 0.40 (hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21 (t, J = 7.4 Hz, 2H), 7.16 – 6.92 (m, 6H), 2.89 (s, 4H), 2.36 (s, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 141.9, 137.9, 129.3, 128.3, 126.7, 125.4, 38.0, 21.4; LRMS (EI$^+$): *Calcd.* for $C_{16}H_{18}$ [M$^+$]: 210.14, found 210.20.

1,2-bis(3-methoxyphenyl)ethane (**2f**).[38] Isolated as a white solid (113.2 mg, 0.47 mmol, 70%) via flash column chromatography with a 20:1 mixture of hexanes/ethyl acetate as the eluent; R_f = 0.48 (20:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 – 7.16 (m, 1H), 6.88 – 6.72 (m, 2H), 3.80 (s, 2H), 2.93 (s, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 159.7, 143.4, 129.3, 120.9, 114.2, 111.3, 55.1, 37.9; LRMS (EI$^+$): *Calcd.* for $C_{16}H_{18}O_2$ [M$^+$]: 242.13, found 242.20.

1,2-bis(3-fluorophenyl)ethane (**2g**).[39] Isolated as a white solid (64 mg, 0.29 mmol, 44%) via flash column chromatography with hexanes as the eluent; R_f = 0.40 (hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (td, J = 7.7, 1.6 Hz, 2H), 7.25 – 7.20 (m, 2H), 6.93 – 6.85 (m, 6H), 2.91 (s, 4H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 162.9 (d, J_{CF} = 245.3 Hz), 143.8 (d, J_{CF} = 7.1 Hz), 129.8 (d, J_{CF} = 8.5 Hz), 124.1 (d, J_{CF} = 2.8 Hz), 115.3 (d, J_{CF} = 20.9 Hz), 113.0 (d, J_{CF} = 21.3 Hz), 37.2 (d, J_{CF} = 1.8 Hz); LRMS (EI$^+$): *Calcd.* for $C_{14}H_{12}F_2$ [M$^+$]: 218.09, found 218.20.

1,2-di-o-tolylethane (**2h**).[39] Isolated as a white solid (73 mg, 0.35 mmol, 52% yield via flash column chromatography with hexanes as the eluent; R_f = 0.40 (hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19 – 7.17 (m, 8H), 2.89 (s, 4H), 2.35 (s, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 140.2, 135.9, 130.2, 128.9, 126.13, 126.0, 34.2, 19.3; LRMS (EI$^+$): *Calcd.* for $C_{16}H_{18}$ [M$^+$]: 210.14, found 210.20.

1,2-bis(2-methoxyphenyl)ethane (**2i**).[38] Isolated as a white solid (129 mg, 0.53 mmol, 80%) via flash column chromatography with a 20:1 mixture of hexanes/ethyl acetate as the eluent; R_f = 0.40 (20:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (td, J = 7.7, 1.6 Hz, 2H), 7.12 (dd, J = 7.2, 1.8 Hz, 2H), 6.89-6.72 (m, 4H), 3.82 (s, 6H), 2.90 (s, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 157.6, 130.9, 129.9, 127.90, 120.2, 110.2, 55.3 30.5. LRMS (EI$^+$): *Calcd.* for $C_{16}H_{18}O_2$ [M$^+$]: 242.13, found 242.20.

1,2-bis(2-fluorophenyl)ethane (**2j**).[39] Isolated as a white solid (79 mg, 0.36 mmol, 54%) via flash column chromatography with hexanes as the eluent; R_f = 0.40 (hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 – 7.13 (m, 4H), 7.06 – 7.02 (m, 4H), 2.97 (s, 4H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.2 (d, J_{CF} = 245.0 Hz), 130.7 (d, J_{CF} = 5.1 Hz), 127.8 (d, J_{CF} = 8.1 Hz), 123.9 (d, J_{CF} = 3.7 Hz), 115.2 (d, J_{CF} = 22.0 Hz), 112.9 (d, J_{CF} = 21.1 Hz), 29.7; LRMS (EI$^+$): *Calcd.* for $C_{14}H_{12}F_2$ [M$^+$]: 218.09, found 218.20.

1,2-bis(benzo[*d*][1,3]dioxo-5-yl)ethane (**2k**).[41] Isolated as a white solid (110 mg, 0.4 mmol, 61%) via flash column chromatography with a 12:1 mixture of hexanes/ethyl acetate as the eluent. R_f = 0.40 (10:1 Hex/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.70 (d, J = 7.8, 2H), 6.64 (d, J = 1.7, 2H), 6.58 (dd, J = 7.9, 1.8, 2H), 5.90 (s, 4H), 2.77 (s, 4H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 147.5, 145.7, 135.5, 121.2, 108.9, 108.1, 100.8, 37.9; LRMS (EI$^+$): *Calcd.* for $C_{16}H_{14}O_4$ [M$^+$]: 270.09, found 270.20.

1,2-bis(4-(trifluoromethyl)phenyl)ethane (**2l**).[41] Isolated as a white solid (32 mg, 0.1 mmol, 15%) via flash column chromatography with hexanes as the eluent; R_f = 0.47 (hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (d, J = 8.0 Hz, 4H), 7.24 (d, J = 7.8 Hz, 4H), 2.98 (s, 4H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 145.0, 128.7, 128.5, 125.3, 37.2; LRMS (EI$^+$): *Calcd.* for $C_{16}H_{12}F_6$ [M$^+$]: 318.08, found 318.20.

1,2-bis(4-(*tert*-butyl)phenyl) ethane (**2m**).[39] Isolated as a white solid (131 mg, 0.45 mmol, 67%) via flash column chromatography with hexanes as the eluent; R_f = 0.40 (hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (d, J = 8.3 Hz, 4H), 7.18 (d, J = 8.2 Hz, 4H), 2.89 (s, 4H), 1.32 (s, 18H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 148.7, 139.0, 128.0, 125.2, 37.4, 34.4, 31.4; LRMS (EI$^+$): *Calcd.* for $C_{22}H_{30}$ [M$^+$]: 294.23, found 294.30.

1-(*tert*-butyl)-4-methylbenzene (**4m**).[42] The reduced product (**4m**) was also isolated a white solid (9.5 mg, 0.048 mmol, 5%); R_f = 0.50 (hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (d, J = 8.3 Hz, 2H), 7.11 (d, J = 8.1 Hz, 2H), 2.31 (s, 3H), 1.30 (s, 9H).

1,2-di(naphthalen-2-yl)ethane (**2n**).[41] Isolated as a white solid (0.47, 132 mg, 70%) via flash column chromatography with a 20:1 mixture of hexanes/ethyl acetate as the eluent.; R_f = 0.34 (20:1 hexanes/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 – 7.73 (m, 6H), 7.66 (s, 2H), 7.47 – 7.40 (m, 4H), 7.36 (d, J = 8.4 Hz, 2H), 3.18 (s, 4H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 139.2, 133.6, 132.1, 127.9, 127.6, 127.5, 127.4, 126.5, 126.0, 125.2, 38.0. LRMS (EI$^+$): *Calcd.* for $C_{22}H_{18}$ [M$^+$]: 282.14, found 282.20.

2-methylnaphthalene (**4n**).[43] The reduced product (**4n**) was also isolated as a colorless oil (25 mg, 0.17 mmol, 15%) with hexanes; R_f = 0.4 (hexanes/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 – 7.72 (m, 3H), 7.60 (s, 1H), 7.41(d, J = 6.9 Hz, 2H), 7.31 (d, J = 8.4 Hz, 1H), 2.51 (s, 3H).

1,2-di(naphthalen-1-yl)ethane (**2o**).[40] Isolated as a white solid (105 mg, 0.37 mmol, 56%) via flash column chromatography with a 20:1 mixture of hexanes/ethyl acetate as the eluent; R_f = 0.34 (20:1 hexanes/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (d, J = 8.0 Hz, 2H), 7.89 (dd, J = 8.0, 1.6 Hz, 2H), 7.75 (dd, J = 8.1, 1.3 Hz, 2H), 7.58 – 7.46 (qd, J = 7.0, 1.6 Hz, 4H), 7.41 (t, J = 7.5 Hz, 2H), 7.35 (dd, J = 7.0, 1.4 Hz, 2H), 3.52 (s, 4H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 138.1, 134.0, 131.9, 128.9, 126.9, 126.0, 125.7, 125.6, 123.7, 34.1; LRMS (EI$^+$): *Calcd.* for $C_{22}H_{18}$ [M$^+$]: 282.14, found 282.20.

1-methylnaphthalene (**4o**).[43] The reduced product (**4o**) was also isolated as a colorless oil (43 mg, 0.3 mmol, 23% yield) with hexanes; R_f = 0.4 (hexanes/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, J = 8.0 Hz, 1H), 7.86 (dd, J = 8.0, 1.6 Hz, 1H), 7.72 (dd, J = 8.1, 1.3 Hz, 2H), 7.55 – 7.47 (qd, J = 7.0, 1.6 Hz, 2H), 7.39 (t, J = 7.5 Hz, 1H), 7.33 (dd, J = 7.0, 1.4 Hz, 1H), 2.71 (s, 3H).

Dimethyl 4,4'-(ethane-1,2-diyl)dibenzoate (**2p**).[44] Isolated as a white solid (7 mg, 0.035 mmol, 4%) via flash column chromatography with a 4:1 mixture of hexanes/ethyl acetate as the eluent; R_f = 0.35 (5:1 hexanes/EtOAc), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, J = 8.3 Hz, 4H), 7.18 (d, J = 8.3 Hz, 4H) 3.89 (s, 6H), 2.97 (s, 4H).

Methyl-4-methylbenzoate (**4p**).[45] The reduced product (**4p**) was also isolated as colorless oil (79 mg, 0.53 mmol, 40%) with a 10:1 mixture of hexanes/ethyl acetate as the eluent; R_f = 0.34 (10:1 hexanes/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, J = 7.9 Hz, 2H), 7.22 (d, J =

7.9 Hz, 2H), 3.88 (s, 3H), 2.39 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 167.2, 143.5, 129.6, 129.1, 129.0, 127.5, 51.9, 21.6.

4-methylbenzonitrile (**4q**).[46] The reduced product (**4q**) was isolated as a colorless oil (61 mg, 0.52 mmol, 83%) with a 20:1 mixture of hexanes/ethyl acetate as the eluent; R_f = 0.6 (15:1 hexanes/EtOAc); ^1H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, *J* = 8.2 Hz, 2H), 7.23 (d, *J* = 8.5 Hz, 2H), 2.38 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 143.7, 132.0, 129.8, 119.1, 109.3, 21.8.

1,2-bis(3,5,6-trimethoxyphenyl)ethane (**2r**).[38] Isolated as an off-white solid (36 mg, 0.1 mmol, 15%) via flash column chromatography with a 1:1 mixture of hexanes/ethyl acetate as the eluent; R_f = 0.40 (1:1 hexanes/EtOAc); ^1H NMR (400 MHz, $CDCl_3$): δ 6.37 (s, 4H), 3.83 (s, 18H), 2.86 (s, 4H), $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 153.1, 137.4, 136.2, 105.5, 60.9, 56.1, 38.5; HRMS (ESI^+): *Calcd.* for $C_{20}H_{26}O_6$ $[M+Na]^+$: 385.1627, found 385.1630.

1,2,3-trimethoxy-5-methylbenzene (**4r**).[47] The reduction product (**4r**) was also isolated as a white solid (88 mg, 0.48 mmol, 36%) via flash column chromatography with a 10:1 mixture of hexanes/ethyl acetate as the eluent; $\mathbf{R}_f$ = 0.48 (10:1 Hex/EtOAc); ^1H NMR (400 MHz, $CDCl_3$): δ 6.38 (s, 2H), 3.83 (s, 6H), 3.81 (s, 3H), 2.30 (s, 3H), 2.34 (s, 3H).

Procedure for Ni-catalyzed carboxylation of N,N-dimethylbenzyl amine.

A 10 mL oven dried round bottom flask equipped with a magnetic stir bar was evacuated and charged with catalyst $NiBr_2$·glyme (22 mg, 0.067 mmol) and 2,9-dibutyl-4,7-dimethyl-1,10-phenanthroline (32 mg, 0.15 mmol) under positive pressure of nitrogen. Degassed DMF (3.4 mL, 0.4 M) was added via a syringe. Manganese (74 mg, 1.32 mmol), benzyl amine (1.34 mmol) and trimethylphosphate were added to the mixture, and the entire mixture evacuated and refilled three times under carbon-dioxide atmosphere. The flask was equipped with a condenser and the entire mixture stirred under an atmosphere of CO_2 at 100 °C (oil bath) for 24 h. The mixture was then cooled to room temperature, and carefully diluted with 2M HCl. The organic layer was extracted with ethyl acetate (20 mL × 3) and the combined extract washed with brine (10 mL) and then dried over Na_2SO_4. The crude product was purified by flash column chromatography with a 4:1 mixture of hexanes/ethyl acetate. **7** was isolated as an off-white solid (32 mg, 0.26 mmol, 35%). Phenylacetic acid (**7**).[13c] ^1H NMR (500 MHz, $CDCl_3$): δ 11.29 (b, 1H), 7.49 – 7.14 (m, 5H), 3.68 (s, 2H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 178.2, 134.0, 133.4, 130.3, 129.5, 128.8, 127.5.1, 41.3.

General procedure for preparation of di, tri and tetra- benzyl ammonium iodides.

*Synthesis of **8**, **9**, **10**, **14***: Amine (1 equiv.) and alkyl iodide (1.5 equiv.) or alkytosylate were dissolved in acetonitrile (1 M) in a round bottom flask. The entire mixture was refluxed (90°C in an oil bath) for 12 h. The resultant precipitate was filtered and the filtrate washed with ether (10 mL × 4) to afford the corresponding iodide salt (see Table S2 in the SI).

***N*-benzyl-*N,N*-dimethyl-phenylmethanaminium iodide** (**8**). Reaction performed with 22 mmol of amine in 22 mL acetonitrile. **8** was isolated as an off white solid (1.8 g, 35%); mp: 189–190 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.69 (d, *J* = 7.3 Hz, 4H), 7.45 – 7.39 (m, 6H), 5.18 (s, 4H), 3.14 (s, 6H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 133.4, 130.8, 129.2, 127.1, 67.2, 48.2; HRMS (ESI^+): *Calcd.* for $C_{16}H_{20}N$ [M-I]: 226.1596, found 226.1599.

***N,N,N*-tribenzyl-methyl ammonium iodide** (**9**). Reaction was performed with 7.0 mmol of amine in 7 mL acetonitrile to afford a white solid (1.3 g, 42%); mp: 180–181 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.66 (d, *J* = 6.9 Hz, 6H), 7.56 – 7.43 (m, 9H), 5.08 (s, 6H), 2.80 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 133.5, 130.9, 129.4, 126.4, 64.6, 45.2; HRMS (ESI^+): *Calcd.* for $C_{22}H_{24}N$ [M-I]: 302.1903, found 302.1914.

***N,N,N,N*-tetrabenzyl-methyl ammonium tosylate** (**10**). Reaction performed with 3.5 mmol of amine in 4 ml acetonitrile, and **10** was isolated as a white solid (0.7 g, 37%). ^1H NMR (500 MHz, $CDCl_3$): δ 7.66 (d, *J* = 6.9 Hz, 6H), 7.56 – 7.43 (m, 9H), 4.25 (s, 4H), 4.24 (s, 4H), 2.80 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 139.9, 131.2, 129.9, 129.4, 128.8,126,2, 66.0, 21.4; HRMS (ESI^+): *Calcd.* for $C_{21}H_{22}N$ [M-$PhCH_2OTs$+H]$^+$: 288.1752, found 288.1755.

***N*-benzyl-N,N-dimethyl-1-(p-tolyl)methaneammonium iodide** (**14**). Reaction was performed with 6.7 mmol of amine in 7 mL acetonitrile to afford a white solid filtration (1.4 g, 57%). mp: 189–190 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 7.65 (d, *J* = 7.2 Hz, 2H), 7.51 (d, *J* = 7.7 Hz, 2H), 7.45 – 7.38 (m, 3H), 7.19 (d, *J* = 7.7 Hz, 2H), 5.12 (s, 2H), 5.14 (s, 2H), 5.10 (s, 2H), 3.10 (s, 6H), 2.34 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 141.1, 133.4,133.3, 130.7, 129.8, 129.2, 127.1, 124.0, 67.1, 67.0, 48.2, 21.4; HRMS (ESI^+): *Calcd.* for $C_{17}H_{22}N$ [M-I]: 240.1747, found 240.1749.

General procedure for preparation of dibenzyl amines.

*Synthesis of **11**, **13***: Amine (23 mmol), alkyl iodide (26 mmol) were dissolved in acetonitrile (230 mL, 0.1 M) in a round bottom flask. *N,N*-diisopropylethylamine (1.5 equiv.) was then added. The entire mixture was stirred at rt for 2 h. Solvent was then removed *in vacuo* and the resultant residue dissolved in dichloromethane (20 mL). The organic layer was subsequently washed once with water (5 mL) and the aqueous layer washed with dichloromethane (10 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4, filtered and the solvent removed again *in vacuo*. The crude mixture was purified by flash column chromatography to afford pure amine compound.

***N,N*-dibenzyl-methylamine** (**11**). Isolated as a light-yellow oil (4.36 g, 90%) with a mixture of 20:1 hexanes/ethyl acetate. ^1H NMR (500 MHz, $CDCl_3$): δ 7.48 – 7.34 (m, 10H), 3.62 (s, 4H), 2.29 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 139.6, 129.1, 128.4, 127.2, 62.1, 42.5; HRMS (ESI^+): *Calcd.* for $C_{15}H_{17}N$ $[M+H]^+$: 212.1439, found 212.1439.

***N,N*-benzyl-N-methyl-1-(p-tolyl)methaneamine** (**13**). Isolated as a colorless oil (4.2 g, 81%) with a mixture of 20:1 hexanes/ethyl acetate; ^1H NMR (500 MHz, $CDCl_3$): δ 7.49 (d, *J* = 8.5 Hz, 2H), 7.44 (t, *J* = 8.4 Hz, 2H), 7.39 – 7.34 (m, 3H), 7.26 (d, *J* = 7.8 Hz, 2H), 3.63 (s, 2H), 3.62 (s, 2H), 2.46 (s, 3H), 2.30 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 139.6, 136.5, 136.4, 129.1, 129.0, 128.3, 61.9, 61.8, 42.3, 21.3; HRMS (ESI^+): *Calcd.* for $C_{16}H_{20}N$ $[M+H]^+$: 226.1596, found 226.1599.

Synthesis of 2,9-dibutyl-4,7-dimethyl-1,10-phenanthroline, **L5**

To a solution of 4,7-dimethyl-1,10-phenanthroline (480 mg, 2.3 mmol) in anhydrous toluene (11.5 mL) at 0 °C was added slowly *n*-BuLi (6 mL, 1.6 M, 9.6 mmol) over 5 mins. The entire mixture was allowed to slowly warm up to room temperature and further stirred for 12 h at this temperature. The reaction was then quenched by addition of water (30 mL) and the organic layer extracted twice with dichloromethane (30 mL × 2). The combined organic extract was stirred with activated MnO_2 (1.24 g, 14.24 mmol) for 4 h. The slurry was then filtered through a pad of Celite and solvent removed under reduced pressure. The crude extract was purified by flash column chromatography with a mixture of 10:1 hexane/ethyl acetate as the eluent. L**5** was obtained as a pale-yellow solid (530 mg, 69%).

2,9-dibutyl-4,7-dimethyl-1,10-benzyl-phenanthroline (**L5**).[13c] ^1H NMR (500 MHz, $CDCl_3$): δ 7.93 (s, 2H), 7.34 (s, 2H), 3.16 (t, *J* = 7.9 Hz, 4H), 2.75 (s, 6H), 1.93 – 1.51 (m, 4H), 1.52 (h, *J* = 7.4 Hz, 4H), 1.00 (t, *J* = 7.4 Hz, 6H).

General procedure for Ni-catalyzed iterative alkyl group transfer from amines and ammonium salts with and without trimethylphosphate

A 25 mL oven dried round bottom flask equipped with a magnetic stir bar was evacuated and charged with catalyst NiI_2 (42 mg, 0.134 mmol) and Xantphos (115 mg, 0.2 mmol) under positive pressure of nitrogen. Degassed DMA (3.4 mL, 0.4 M) was added via a syringe and the entire mixture stirred for 5 min at 120 °C (oil bath), after which the solution became homogeneous and the color changed from grey to red. Mn (219 mg, 4 mmol), either the benzyl amine or the corresponding ammonium salt (1.34 mmol), or with or without trimethyl phosphate (5.36 mmol) were added to the mixture. The flask was equipped with a condenser and the entire mixture stirred under nitrogen at 120 °C (oil bath) for 24 h. The mixture was the cooled to room temperature and subsequently extracted with diethyl ether (20 mL × 3). The combined organic extract was washed with water (20 mL × 2), followed by brine (10 mL). The organic layer was then dried over Na_2SO_4, filtered and solvent removed under reduced pressure. The crude mixture was purified by flash column chromatography on silica gel with hexanes as the eluent. Yield

reported as an average of at least two independent runs. Yield of isolated diphenyl ethane (**2a**) was calculated based on total possible benzyl transfers with or without trimethyl phosphate additive.

ASSOCIATED CONTENT

Supporting Information

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

Materials and methods, general experimental procedures, characterization data and spectra for the synthesis of substrates and ligands, and reaction analysis by ^{1}H NMR and GC-MS (PDF)

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Notes

The authors declare no competing financial interest.

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