JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

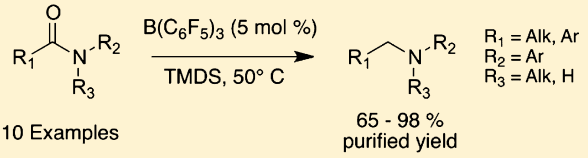
Metal-Free Reduction of Secondary and Tertiary *N*-Phenyl Amides by Tris(pentafluorophenyl)boron-Catalyzed Hydrosilylation

Ryan C. Chadwick, Vladimir Kardelis, Philip Lim, and Alex Adronov*

Department of Chemistry, McMaster University, 1280 Main Street West, Hamilton, Ontario L8S 4M1, Canada

Supporting Information

ABSTRACT: Tris(pentafluorophenyl)boron $B(C_6F_5)_3$ is an effective catalyst for the hydrosilylative reduction of tertiary and *N*-phenyl secondary amides. It allows for the mild reduction of a variety of these amides in near quantitative yield, with minimal purification, at low temperatures, and with short reaction times. This reduction shows functional group tolerance for alkenes, nitro groups, and aryl halides, including aryl iodides.



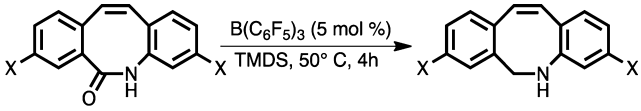
Mild reduction of the amide functionality to the corresponding amine is a valuable transformation in organic synthesis. Traditionally, the most common procedures for the transformation of amides to amines have involved the use of metal hydride reagents in stoichiometric amounts.[1] These reagents are not generally selective and result in byproduct mixtures that are difficult to purify. More recently, catalytic reductions of amides have received significant attention. Although ideal, reports of direct catalytic hydrogenation of amides to amines are quite rare, and limited in scope and versatility. Most early reports utilized very harsh conditions and were substrate-specific.[2] A 2007 report by Magro et al. utilized a ruthenium-triphos catalyst to achieve a general reduction of amides, but the reaction required high temperatures (164 °C) and moderately high pressures (40 bar H_2).[3] More recently, a lower pressure (10 mbar), but higher temperature (200 °C), optimized protocol that is effective for reducing secondary and aryl amides has been reported.[4] Burch et al. succeeded in developing a reduction that operated at lower temperatures and pressures (120 °C, 20 bar, H_2), but the substrate scope was not widely explored.[5] Most recently, Stein and Breit developed a Pt/Re system that is general and high yielding, but still requires moderately high temperatures (160 °C, 30 bar H_2).[2] In addition, these reductions generally exhibit insufficient functional group tolerance, precluding the presence of alkenes and other easily hydrogenated functionalities. It should also be noted that mild methods are available to reduce amides to other functionalities, such as alcohols[6] and aldehydes.[7]

In contrast, catalytic hydrosilylation as a methodology for amide reduction has received significant recent attention, and a number of reports utilizing transition-metal catalysts (Rh,[8] Mn,[9] Ru,[9−11] Os,[9] Ir,[9,12] Pt,[9,13] Pd,[9] Re,[9] Fe,[14−16] In[17]) have appeared. However, many of these catalysts are expensive, and reaction conditions involve high temperatures that decrease compatibility with thermally sensitive functional groups. More recently, Beller and co-workers have developed amide reduction methods using Cu,[18] Fe,[15] and Zn[19,20] containing Lewis acids that overcome most of the limitations of previous methods. For example, the reduction of a wide variety of secondary and tertiary amides was demonstrated with remarkable substrate scope and functional group tolerance using $Zn(OTf)_2$.[19]

Alternatively, the state-of-the-art "metal-free" method relies on the use of triflic anhydride and the "Hantzsch" ester to facilitate the reduction.[21] This method is remarkable, resulting in high yields of amine without the need for column chromatography. Charette and co-workers demonstrated the utility of this approach with both tertiary[21] and secondary[22] amides, which allowed formation of imines, amines, or aldehydes through control of the workup procedure following formation of the intermediate iminium triflate ion.[22] While synthetically ideal from a control and tolerance perspective, this procedure requires expensive cofactors, highly reactive and expensive triflic anhydride, and cryogenic temperatures, making it somewhat onerous.

Recently, we attempted to reduce the secondary amides **1** and **2** (Scheme 1) by a number of conventional methods.

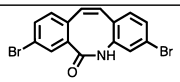
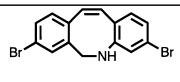
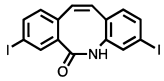
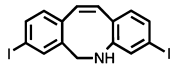
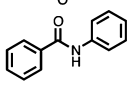
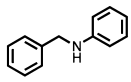
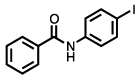
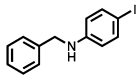
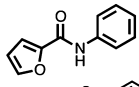
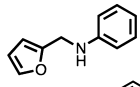
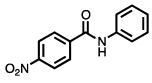
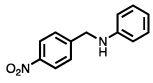
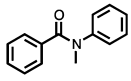
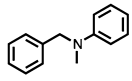
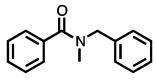
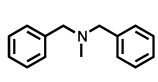
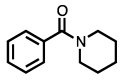
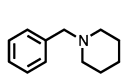
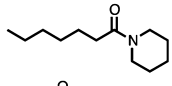
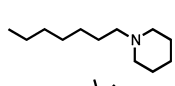
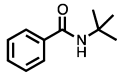
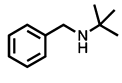
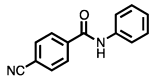
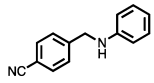
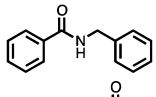
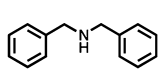
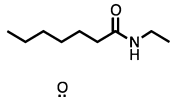
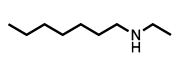
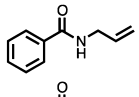
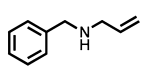
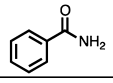
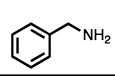
Scheme 1. Reduction of Model Amides 1 and 2



However, the combination of functional groups within these structures made it difficult to achieve high-yielding reduction.[23] In our attempts, $LiAlH_4$ rapidly dehalogenated the aryl halide groups, while DIBAL-H allowed the reduction of the dibromide in modest yield (ca. 50%), but also dehalogenated the diiodide. Surprisingly, in situ generated alane (AlH_3) reduced the double bond. Attempts to use borohydrides or boranes failed, due

Received: June 10, 2014
Published: July 17, 2014

Table 1. Amines from the Hydrosilylation of Amides[a,b,c]

Entry	Amide	Amine	Conditions	Yield (%)
1			50 °C, 4 h	92
2			50 °C, 1.5 h	86
3			50 °C, 1 h	96
4			50 °C, 1.5 h	>98
5			r.t., 2 h	91
6			50 °C, 4 h	92
7			r.t., 1.5 h	>98
8			50 °C, 1 h	>98
9			50 °C, 1 h	97
10			130 °C, 1d	65
11			110 °C, 1d	0[b]
12			50 °C, 1 h	0[c]
13			130 °C, 1d	0[b]
14			130 °C, 1d	0[b]
15			130 °C, 1d	0[b]
16			130 °C, 1d	0[b]

[a]Conditions: amide (1 mmol), TDMS (4 mmol, 8 equiv Si-H), $B(C_6F_5)_3$ (0.05 mmol as 0.05 M solution in toluene), toluene (3 mL), $Ar_{(g)}$. [b]Only starting materials were isolated. [c]Multiple products.

either to insufficient reactivity or to reduction of the alkene functionality. We thus turned to the use of $Zn(OTf)_2$ and tetramethyldisiloxane (TMDS) in toluene, as developed by Das et al.[19] These conditions were effective for the reduction of both **1** and **2**, but required unusually high temperatures. No reduction was observed at 110 °C (over 3 days), and even at elevated temperatures of 130 °C, reaction times were long (48 h) and the use of a high-pressure vessel was required. Attempts to reduce the reaction time by heating to 150 °C drastically reduced the yield. Additionally, we hypothesize that catalyst decomposition occurred during the course of the reaction (some black precipitate was produced at high temperature), resulting in partial dehalogenation of the substrate, and although yields were acceptable (ca. 80%), purification from these dehalogenated side products was generally difficult.

To circumvent these issues, we turned our attention to other, more powerful Lewis acids for this hydrosilylative reduction. Tris(pentafluorophenyl)boron ($B(C_6F_5)_3$) is a powerful Lewis acid, having activity intermediate to BCl_3 and BF_3, yet it is relatively water stable.[24−27] Piers and colleagues, among others, have described the use of this catalyst for the hydrosilylation of many functional groups, including alcohols and ethers,[28] carbonyl groups,[29−31] as well as imines and nitriles.[27,32,33] In addition, it has been shown to be particularly effective for the silylation of various alcohols,[34] as well as the condensation of hydrosilanes and alkoxysilanes to produce branched and linear silicones with well-defined structures (Piers−Rubinsztajn

dx.doi.org/10.1021/jo501299j | J. Org. Chem. 2014, 79, 7728−7733

reaction).[35−39] It is also capable of a rapid cross-linking reaction as an alternative room-temperature vulcanization method for making silicone rubbers and silicone foams.[40] However, to the best of our knowledge, only one report exists in the literature detailing the use of $B(C_6F_5)_3$ for the hydrosilylative reduction of amides.[41] This report utilized diphenylsilane as the reducing agent for three aliphatic *N*-aryl amides. Considering the vast literature on the reduction of imines, nitriles, and carbonyl groups with $B(C_6F_5)_3$, including in-depth discussions of the reduction mechanism,[27,29,32,33] we found it surprising that the scope of the corresponding amide reduction has not been explored, nor was the reaction protocol optimized.[41]

In our experiments, we rapidly discovered that the use of 5 mol % $B(C_6F_5)_3$ as a substitute for $Zn(OTf)_2$ in the reduction of **1** and **2** to the corresponding amines proceeded in near quantitative yield at mild temperatures (50 °C, Table 1). The use of less catalyst (1−2 mol %) prevented complete reaction in a reasonable amount of time, while the addition of more catalyst (10 mol %) decreased the reaction time markedly, to less than 1 h (though 5% was always enough to ensure complete conversion). It is known that $B(C_6F_5)_3$ forms complexes with imine and amine reagents, and we expect the product poisons the catalyst to some degree, dramatically slowing the reaction when low catalyst loading is used.[42] Most notably, when sufficient catalyst quantities are present, no side products appear to be produced, and purification requires only standard flash chromatographic purification to remove excess silane, spent siloxane, and the residual boron catalyst.

As this method was mild, rapid, and capable of cleanly reducing amides **1** and **2**, we set out to investigate its scope. The functional group tolerance of $B(C_6F_5)_3$ is well-established,[29,30,34,42] so our primary aim was to determine the structural variability of amides that could be reduced by this methodology. The structures of the different amides that were attempted, along with the corresponding amines, are presented in Table 1.

Generally, this method was capable of reducing *N*-phenyl amides in excellent yield (Table 1, entries 1−7) and was also effective at reducing tertiary benzyl amides (Table 1, entry 8). These substrates were all reduced in high yield in 4 h or less. The reaction rate for these substrates appeared to be primarily controlled by their solubility. Entries 1 and 6 involved amide structures that were poorly soluble in toluene and, therefore, required a 4 h reaction time to reach completion. The other *N*-phenyl amides in the first seven entries of Table 1 required 1.5 h or less at 50 °C. The presence of halogens, or electron-withdrawing substituents did not substantially affect the reaction rate or yield. Entry 5 was significantly faster than the other *N*-phenyl amides, only requiring 2 h at room temperature. This increased reaction rate may result from the extra coordination to boron afforded by the furan oxygen.[32] Heptane was also a suitable solvent for these reductions, but all reactions were found to be slower, again due to the reduced solubility in this solvent. It should be noted that, despite longer reaction times for the less soluble structures, product yields were generally high.

As noted in the previous report,[41] reduction of aliphatic tertiary amides with aromatic substituents on the carbonyl carbon proceeded smoothly (entry 9). However, in the case where aliphatic substituents were present on both sides of the amide, the reductions were more difficult and yields suffered accordingly (entry 10). Interestingly, this method appears to be unable to reduce primary amides or secondary *N*-alkyl, *N*-benzyl, or *N*-allyl amides, though it appears that it is not essential that the system be conjugated through the carbonyl side (entries 11, 13−16).[41] Furthermore, while nitro groups were well-tolerated (entry 6), it was found that nitriles underwent reduction, leading to multiple products (entry 12). In the cases where reduction was not observed, isolation of the starting material allowed for approximately 95% recovery. We speculate the mechanism of reaction follows a similar pathway as the reduction of esters.[42] This differs from the mechanism of $B(C_6F_5)_3$ reduction of imines in that no Si−N bond is formed. Accordingly, we were unable to reduce secondary *tert*-butyl amides, in contrast to results by Blackwell et al. with *tert*-butyl imines.[42]

In order to determine the mechanism of inhibition for secondary *N*-alkyl amides, we attempted a reduction of *N*-benzylbenzamide using 25% loading of $B(C_6F_5)_3$. We were able to obtain ca. 70% recovery of our starting material; however, we also observed a highly polar product by TLC (R_f = 0.2, 1:9 MeOH:EtOAc). When isolated via chromatography (ca. 15% yield), the solid product produced a ^{1}H NMR spectrum consistent with dibenzylamine. This is consistent with the production of a strong $B(C_6F_5)_3$ adduct. In fact, the literature confirms that the adducts of $B(C_6F_5)_3$ are especially strong due to a bifurcated F−H−F hydrogen bond between the amine proton and two of the ring fluorine atoms.[43−45] On the basis of this evidence, we hypothesize that the variation in rate across amide types is primarily dependent on the strength of the amine−$B(C_6F_5)_3$ complex. *N*-Phenyl amines are considerably less basic than aliphatic amines, and would be expected to form a much weaker complex. Tertiary amines are more basic, but lack the presence of an amine N-hydrogen to form additional hydrogen bonds. Secondary *N*-alkyl amines form strong bifurcated H-bonds with the $B(C_6F_5)_3$ ring fluorides,[43] and we speculate that this H-bonded complex is too strong to permit catalyst turnover, thus poisoning the catalyst after a single cycle.

Lastly, reductions of *N*-phenylamide (**3**) with silanes other than TMDS were also successful. Diphenylsilane (DPS), diphenylmethylsilane (DPMS), and polymethylhydrosiloxane (PMHS, Gelest; M_n: ca. 2 kDa) were equally efficient for these reductions (Table 2). However, in each case, purification was less facile. The phenyl silanes had similar R_f values to the product amines, due to their more polar nature. While ideal from a cost standpoint and its status as an industrial byproduct, the use of PMHS as a reducing agent produces a cross-linked gel that makes product isolation tedious.

Table 2. Product Yield from Hydrosilylative Reduction Using Different Silanes[a]

silane	yield %
TMDS	96
DPS	95
DPMS	95
PMHS	80

[a]Conditions: *N*-phenylamide **3** (1 mmol), silane (4 mmol), $B(C_6F_5)_3$ (0.05 mmol as 0.05 M solution in toluene), toluene (3 mL), $Ar_{(g)}$.

In conclusion, the use of $B(C_6F_5)_3$ leads to efficient, mild, and selective reduction of both secondary and tertiary *N*-phenyl amides, as well as conjugated tertiary amides. The scope and limitations for the reductions of amides appear to mirror those found in the literature for imines.[42] In particular, we have found

dx.doi.org/10.1021/jo501299j | J. Org. Chem. 2014, 79, 7728−7733

this to be very useful in the reduction of amides in the presence of alkenes and aryl iodides.

EXPERIMENTAL SECTION

General. All reactions were run under an argon atmosphere. The toluene used for the reductions was dried via an alumina column in a solvent purification system. All amides, except for entries **1** and **2**, were synthesized from their respective amines and acyl chlorides using a modified literature method.[19] Amide **1** was synthesized via a previously reported procedure.[23] An analogous synthesis of amide **2**, following modified literature procedures, is reported below. All yields are isolated yields. Solutions were deoxygenated by sparging with argon while sonicating. All NMR chemical shifts (δ) are reported in ppm and coupling constants (J) in Hz.

General Procedure for the Reduction of Amides. A dry 50 mL Schlenk tube, or round-bottom flask, was charged with the amide (1 mmol) and dry toluene (3 mL). The mixture was degassed with argon in an ultrasonicator for 15 min before adding TMDS (537 mg, 4 mmol). While stirring at 50 °C, a 0.05 M degassed solution of $B(C_6F_5)_3$ in dry toluene (1 mL, 0.05 mmol) was added in two aliquots, over 30 min, resulting in gas evolution. The reaction was monitored by thin-layer chromatography. Upon completion, the remaining toluene was evaporated under reduced pressure, leaving behind a crude mixture that was purified via a short basic alumina column eluting with hexanes to remove silyl compounds, followed by CH_2Cl_2 to elute product.

Procedure for the Reduction of 1-(Piperidin-1-yl)heptan-1-one. A dry pressure vessel of appropriate size was charged with 1-(piperidin-1-yl)heptan-1-one (197 mg, 1 mmol), $B(C_6F_5)_3$ (25.6 mg, 0.05 mmol), and toluene (4 mL). The mixture was degassed with argon in an ultrasonicator for 15 min before adding TMDS (537 mg, 4 mmol). The pressure vessel was sealed with a stir bar and submerged in an oil bath at 130 °C for 24 h. The vessel was removed from the oil bath and allowed to cool to room temperature before being opened. After evaporating the remaining toluene under reduced pressure, the oily residue was purified via column chromatography using silica gel passivated with Et_3N in EtOAc/*n*-hexanes 1:4.

Synthesis of Amide 2:[23] *3,7-Diiodo-10,11-dihydro-dibenzo[a,d]cyclohepten-5-one.*[46] Dibenzosuberone (10.50 g, 50 mmol), I_2 (16.50 g, 65 mmol), and acetic acid (100 mL) were added to a 500 mL 2-N round-bottom flask equipped with a condenser and addition funnel, forming a red-violet mixture. A mixture of HNO_3 (4 mL) and H_2SO_4 (10 mL) was then added dropwise to the stirring reaction, followed by CCl_4 (5 mL). The reaction was heated and stirred at reflux for 5 h, then partitioned between water (500 mL) and chloroform (500 mL) while molten. The aqueous phase was further extracted with chloroform (3 × 100 mL). The organic phases were combined and washed with 2 M $NaSO_3$ (4 × 150 mL), 5% $NaHCO_3$ (3 × 150 mL), and brine (1 × 150 mL). The organic phase was dried over magnesium sulfate and then filtered and evaporated under reduced pressure to yield a crude reddish solid. The crude material was passed through a silica plug and purified via recrystallization from 1:8 1,4-dioxane/EtOH to yield 6.44 g, 14.0 mmol (28%) of an off-white crystalline solid. ^{1}H NMR (700 MHz; $CDCl_3$): δ 8.29 (d, J = 1.6, 2H), 7.74 (dd, J = 8.0, 1.7, 2H), 6.97 (d, J = 8.0, 2H), 3.12 (s, 4H). ^{13}C NMR (176 MHz; $CDCl_3$): δ 192.5, 141.42, 141.37, 139.7, 139.4, 131.4, 91.8, 34.4. HRMS (ESI+) (m/z) calculated for $C_{15}H_{11}OI_2$ $[M + H]^+$ 460.8899, measured 460.8919.

3,7-Diiodo-5H-dibenzo[a,d][7]annulen-5-one.[47] A mixture of 3,7-diiodo-10,11-dihydro-dibenzo[a,d]cycloheptene-5-one (2.00 g, 4.35 mmol), *N*-bromosuccinimide (1.01 g, 5.65 mmol), benzoyl peroxide (42 mg, 0.17 mmol), and 1,2-dichloromethane (30 mL) was added to a 100 mL round-bottom flask equipped with a reflux condenser. The light brown mixture was stirred at reflux for 4 h and then slowly cooled to room temperature. The precipitate was dissolved in dichloromethane before washing with 5% NaOH (3 × 75 mL), water (1 × 75 mL), and brine (1 × 75 mL). The organic phase was dried over $MgSO_4$ and evaporated under reduced pressure to yield 2.34 g (quant. recovery) of a tan powder that was moved on to the next reaction without purification. Monitoring the reaction by thin-layer chromatography showed the product at R_f = 0.35 (Et_2O/*n*-hexanes, 1:4).

The crude 10-bromo-3,7-diiodo-10,11-dihydro-5*H*-dibenzo[a,d][7]-annulen-5-one (2.34 g, 4.35 mmol), Et_3N (12 mL), and benzene (25 mL) were added to a 100 mL round-bottom flask equipped with a reflux condenser. The light brown mixture was stirred at reflux for 7 h and then slowly cooled to 0 °C and filtered. The light yellow filtered solid was stirred in 1 M HCl (50 mL), filtered, and washed again with water (50 mL), followed by MeOH (20 mL). The crude solid was purified via recrystallization from toluene to yield 1.39 g, 3.00 mmol (70%) of a light yellow crystalline solid. ^{1}H NMR (700 MHz; DMSO): δ 8.36 (s, 2H), 8.11 (d, J = 8.0, 2H), 7.56 (d, J = 6.8, 2H), 7.23 (s, 2H). ^{13}C NMR (176 MHz; DMSO): δ 189.0, 141.1, 138.7, 138.0, 133.9, 133.2, 131.5, 95.8. HRMS (ESI+) (m/z) calculated for $C_{15}H_9OI_2$ $[M + H]^+$ 458.8743, measured 458.8728.

(Z)-3,8-Diiododibenzo[b,f]azocin-6(5H)-one.[48,49] 3,7-Diiodo-5*H*-dibenzo[a,d][7]annulen-5-one (1.39 g, 3.03 mmol) was added to a mixture of H_2NOH·HCl (1.05 g, 15.2 mmol) and pyridine (10 mL) in a 25 mL round-bottom flask equipped with a reflux condenser. The yellow reaction mixture was stirred while refluxing for 4 h and then diluted with CH_2Cl_2 (200 mL). The solution was washed with 5% $HCl_{(aq)}$ (2 × 100 mL) and brine (1 × 100 mL) and then dried over $MgSO_4$ and evaporated under reduced pressure to yield 1.43 g (quant. recovery) of a pale yellow powder. The mildly moisture sensitive compound was used immediately. Monitoring the reaction by thin-layer chromatography showed a single product at R_f = 0.15 (Et_2O/*n*-hexanes, 1:4).

Eaton's reagent (10 mL) was added to a dry 50 mL round-bottom flask containing the crude 3,7-diiodo-5*H*-dibenzo[a,d][7]annulen-5-one oxime (1.43 g, 3.03 mmol). The brown reaction mixture was stirred at 100 °C for 30 min before being slowly cooled to room temperature and quenching via dropwise addition of water (30 mL) over an ice bath. The resulting precipitate was filtered and rinsed with 5% $NaHCO_{3(aq)}$ (2 × 30 mL), followed by MeOH (10 mL). The tan solid was dried under vacuum to a yield of 1.29 g, 2.73 mmol (90%). An analytically pure product can be obtained by recrystallizing from $CHCl_3$. ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.79 (s, 1H), 7.64 (d, J = 8.0, 1H), 7.53 (d, J = 8.9, 2H), 7.46 (s, 1H), 6.86 (m, 2H), 6.77 (t, J = 11.3, 2H). ^{13}C NMR (176 MHz; $CDCl_3$): δ 171.4, 138.9, 137.1, 136.5, 136.2, 136.1, 135.3, 134.6, 133.3, 132.9, 130.7, 129.9, 129.5, 93.2, 93.0. HRMS (ESI+) (m/z) calculated for $C_{15}H_{10}NOI_2$ $[M + H]^+$ 473.8852, measured 473.8842.

Characterization of Amines. *(Z)-3,8-Dibromo-5,6-dihydrodibenzo[b,f]azocine, (1).* Yield: 336 mg, 0.92 mmol (92%), bright yellow crystalline solid. Oxidizes readily to a light orange solid. ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.58 (dd, J = 8.1, 1.7, 1H), 7.56 (s, 1H), 6.98−6.96 (m, 2H), 6.87 (d, J = 8.0, 1H), 6.65 (d, J = 8.2, 1H), 6.50 (d, J = 12.9, 1H), 6.34 (d, J = 12.9, 1H), 5.79 (s, 1H), 4.51 (s, 2H). ^{13}C NMR (176 MHz; $CDCl_3$): δ 146.2, 138.8, 138.6, 138.1, 137.1, 135.4, 132.4, 131.7, 128.22, 128.10, 127.1, 122.5, 93.6, 92.5, 49.1. HRMS (ESI+) (m/z) calculated for $C_{15}H_{12}NBr_2$ $[M + H]^+$ 363.9336, measured 363.9337.

(Z)-3,8-Diiodo-5,6-dihydrodibenzo[b,f]azocine, (2). Yield: 394 mg, 0.86 mmol (86%), bright yellow crystalline solid. Oxidizes readily to a dark orange solid. ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.58 (dd, J = 8.0, 1.7, 1H), 7.55 (s, 1H), 6.91 (dd, J = 8.2, 1.5, 1H), 6.88 (d, J = 8.1, 1H), 6.85 (s, 1H), 6.63 (d, J = 8.2, 1H), 6.46 (d, J = 13.0, 1H), 6.27 (d, J = 13.0, 1H), 4.60 (s, 1H), 4.49 (s, 2H). ^{13}C NMR (176 MHz; $CDCl_3$): δ 147.5, 139.7, 138.7, 138.0, 137.0, 135.8, 132.7, 131.8, 127.5, 127.2, 126.5, 121.5, 93.6, 92.4, 48.8. HRMS (ESI+) (m/z) calculated for $C_{15}H_{12}NI_2$ $[M + H]^+$ 459.9059, measured 459.9072.

N-Benzylaniline, (3). Yield: 176 mg, 0.96 mmol (96%), clear, colorless liquid. ^{1}H NMR (700 MHz; $CDCl_3$): δ 7.40 (d, J = 7.5, 2H), 7.37 (t, J = 7.5, 2H), 7.30 (t, J = 7.2, 1H), 7.21−7.19 (m, 2H), 6.75 (t, J = 7.3, 1H), 6.67−6.66 (m, 2H), 4.35 (s, 2H), 4.09 (s, 1H). ^{13}C NMR (176 MHz; $CDCl_3$): δ 148.2, 139.5, 129.4, 128.8, 127.6, 127.4, 117.7, 113.0, 48.5. HRMS (ESI+) (m/z) calculated for $C_{13}H_{14}N$ $[M + H]^+$ 184.1126, measured 184.1132.

N-Benzyl-4-iodoaniline, (4). Yield: 303 mg, 0.98 mmol (98%), white crystalline solid. Oxidizes readily to a green solid. ^{1}H NMR (700

dx.doi.org/10.1021/jo501299j | J. Org. Chem. 2014, 79, 7728−7733

MHz; $CDCl_3$): δ 7.41 (d, J = 8.8, 2H), 7.35−7.34 (m, 4H), 7.28 (m, 1H), 6.42 (d, J = 8.8, 2H), 4.30 (s, 2H), 4.20 (s, 1H). ^{13}C NMR (176 MHz; $CDCl_3$): δ 147.7, 138.9, 137.9, 128.9, 127.5, 115.3, 78.4, 48.3. HRMS (ESI+) (m/z) calculated for $C_{13}H_{13}NI$ $[M + H]^+$ 310.0093, measured 310.0099.

*N-(Furan-2-ylmethyl)aniline, (**5**).* Yield: 157 mg, 0.91 mmol (91%), clear, colorless liquid. ^1H NMR (700 MHz; $CDCl_3$): δ 7.40 (s, 1H), 7.23 (t, J = 7.9, 2H), 6.79 (t, J = 7.3, 1H), 6.71 (d, J = 7.7, 2H), 6.36 (s, 1H), 6.27 (s, 1H), 4.35 (s, 2H), 4.04 (s, 1H). ^{13}C NMR (176 MHz; $CDCl_3$): δ 152.8, 147.7, 142.0, 129.3, 118.1, 113.2, 110.4, 107.1, 41.5. HRMS (ESI+) (m/z) calculated for $C_{11}H_{12}NO$ $[M + H]^+$ 174.0919, measured 174.0912.

*N-(4-Nitrobenzyl)aniline, (**6**).* Yield: 210 mg, 0.92 mmol (92%), bright yellow liquid. Oxidizes readily to a dark brown liquid. ^1H NMR (700 MHz; $CDCl_3$): δ 8.17 (d, J = 8.6, 2H), 7.51 (d, J = 8.3, 2H), 7.15 (t, J = 8.0, 2H), 6.73 (t, J = 7.3, 1H), 6.57 (d, J = 7.7, 2H), 4.46 (s, 2H), 4.28 (s, 1H). ^{13}C NMR (176 MHz; $CDCl_3$): δ 147.58, 147.39, 147.31, 129.5, 127.8, 124.0, 118.4, 113.1, 47.8. HRMS (ESI+) (m/z) calculated for $C_{13}H_{13}N_2O_2$ $[M + H]^+$ 229.0977, measured 229.0969.

*N-Benzyl-N-methylaniline, (**7**).* Yield: 193 mg, 0.98 mmol (98%), clear, colorless liquid. ^1H NMR (700 MHz; $CDCl_3$): δ 7.35 (t, J = 7.5, 2H), 7.28−7.25 (m, 5H), 6.80 (d, J = 7.8, 2H), 6.75 (t, J = 6.9, 1H), 4.57 (s, 2H), 3.05 (s, 3H). ^{13}C NMR (176 MHz; $CDCl_3$): δ 149.9, 139.1, 129.3, 128.7, 126.99, 126.87, 116.7, 112.5, 56.8, 38.6. HRMS (ESI+) (m/z) calculated for $C_{14}H_{16}N$ $[M + H]^+$ 198.1283, measured 198.1273.

*N-Benzyl-N-methyl-1-phenylmethanamine, (**8**).* Yield: 207 mg, 0.98 mmol (98%), clear, colorless liquid. ^1H NMR (700 MHz; $CDCl_3$): δ 7.37 (d, J = 7.5, 4H), 7.33 (t, J = 7.5, 4H), 7.26−7.24 (m, 2H), 3.53 (s, 4H), 2.20 (s, 3H). ^{13}C NMR (176 MHz; $CDCl_3$): δ 139.5, 129.1, 128.4, 127.1, 62.0, 42.4. HRMS (ESI+) (m/z) calculated for $C_{15}H_{18}N$ $[M + H]^+$ 212.1439, measured 212.1433.

*1-Benzylpiperidine, (**9**).* Yield: 170 mg, 0.97 mmol (97%), clear, colorless liquid. ^1H NMR (700 MHz; $CDCl_3$): δ 7.32−7.30 (m, 4H), 7.25−7.23 (m, 1H), 3.48 (s, 2H), 2.38 (s, 4H), 1.58 (quintet, J = 5.5, 4H), 1.43 (s, 2H). ^{13}C NMR (176 MHz; $CDCl_3$): δ 138.8, 129.4, 128.2, 126.9, 64.0, 54.6, 26.1, 24.5. HRMS (ESI+) (m/z) calculated for $C_{12}H_{18}N$ $[M + H]^+$ 176.1439, measured 176.1438.

*1-Heptylpiperidine, (**10**).* Yield: 119 mg, 0.65 mmol 65%, clear, colorless liquid. ^1H NMR (600 MHz; $CDCl_3$): δ 2.35 (m, 4H), 2.25 (dd, J = 9.2, 6.7, 2H), 1.57 (quintet, J = 5.7, 4H), 1.48−1.46 (m, 2H), 1.41 (m, 2H), 1.29−1.24 (m, 8H), 0.86 (t, J = 7.0, 3H). ^{13}C NMR (176 MHz; $CDCl_3$): δ 59.9, 54.8, 32.0, 29.4, 27.9, 27.1, 26.1, 24.7, 22.8, 14.2. HRMS (ESI+) (m/z) calculated for $C_{12}H_{26}N$ $[M + H]^+$ 184.2065, measured 184.2069.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^1H and ^{13}C NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: adronov@mcmaster.ca. Tel: (905) 525-9140, ext. 23514. Fax: (905) 521-2773.

Notes

The authors declare no competing financial interest

■ ACKNOWLEDGMENTS

Financial support for this work was provided by the Natural Science and Engineering Research Council of Canada (NSERC). R.C.C. is grateful for the support through the Ontario Graduate Scholarships (OGS) program.

■ REFERENCES

(1) Seyden-Penne, J. *Reductions by the Alumino- and Borohydrides in Organic Synthesis*; Wiley-VCH: New York, 1997.
(2) Stein, M.; Breit, B. *Angew. Chem., Int. Ed.* **2013**, *52*, 2231−2234.
(3) Núñez Magro, A. A.; Eastham, G. R.; Cole-Hamilton, D. *J. Chem. Commun.* **2007**, 3154−3156.
(4) Coetzee, J.; Dodds, D. L.; Klankermayer, J.; Brosinski, S.; Leitner, W.; Slawin, A. M. Z.; Cole-Hamilton, D. *J. Chem. Eur. J.* **2013**, *19*, 11039−11050.
(5) Burch, R.; Paun, C.; Cao, X. M.; Crawford, P.; Goodrich, P.; Hardacre, C.; Hu, P.; McLaughlin, L.; Sá, J.; Thompson, J. M. *J. Catal.* **2011**, *283*, 89−97.
(6) Szostak, M.; Spain, M.; Eberhart, A. J.; Procter, D. J. *J. Am. Chem. Soc.* **2014**, *136*, 2268−2271.
(7) Spletstoser, J. T.; White, J. M.; Tunoori, A. R.; Georg, G. I. *J. Am. Chem. Soc.* **2007**, *129*, 3408−3419.
(8) Kuwano, R.; Takahashi, M.; Ito, Y. *Tetrahedron Lett.* **1998**, *39*, 1017−1020.
(9) Igarashi, M.; Fuchikami, T. *Tetrahedron Lett.* **2001**, *42*, 1945−1947.
(10) Matsubara, K.; Iura, T.; Maki, T.; Nagashima, H. *J. Org. Chem.* **2002**, *67*, 4985−4988.
(11) Motoyama, Y.; Mitsui, K.; Ishida, T.; Nagashima, H. *J. Am. Chem. Soc.* **2005**, *127*, 13150−13151.
(12) Cheng, C.; Brookhart, M. *J. Am. Chem. Soc.* **2012**, *134*, 11304−11307.
(13) Hanada, S.; Tsutsumi, E.; Motoyama, Y.; Nagashima, H. *J. Am. Chem. Soc.* **2009**, *131*, 15032−15040.
(14) Sunada, Y.; Kawakami, H.; Imaoka, T.; Motoyama, Y.; Nagashima, H. *Angew. Chem., Int. Ed.* **2009**, *48*, 9511−9514.
(15) Zhou, S.; Junge, K.; Addis, D.; Das, S.; Beller, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 9507−9510.
(16) Das, S.; Wendt, B.; Möller, K.; Junge, K.; Beller, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 1662−1666.
(17) Sakai, N.; Fujii, K.; Konakahara, T. *Tetrahedron Lett.* **2008**, *49*, 6873−6875.
(18) Das, S.; Join, B. I. T.; Junge, K.; Beller, M. *Chem. Commun.* **2012**, *48*, 2683−2685.
(19) Das, S.; Addis, D.; Junge, K.; Beller, M. *Chem.—Eur. J.* **2011**, *17*, 12186−12192.
(20) Das, S.; Addis, D.; Zhou, S.; Junge, K.; Beller, M. *J. Am. Chem. Soc.* **2010**, *132*, 1770−1771.
(21) Barbe, G.; Charette, A. B. *J. Am. Chem. Soc.* **2008**, *130*, 18−19.
(22) Pelletier, G.; Bechara, W. S.; Charette, A. B. *J. Am. Chem. Soc.* **2010**, *132*, 12817−12819.
(23) Chadwick, R. C.; Kardelis, V.; Liogier, S.; Adronov, A. *Macromolecules* **2013**, *46*, 9593−9598.
(24) Jacobsen, H.; Berke, H.; Döring, S.; Kehr, G.; Erker, G.; Fröhlich, R.; Meyer, O. *Organometallics* **1999**, *18*, 1724−1735.
(25) Massey, A. G.; Park, A. J. *J. Organomet. Chem.* **1964**, *2*, 245−250.
(26) Erker, G. *Dalton Trans.* **2005**, 1883−1890.
(27) Piers, W. E.; Chivers, T. *Chem. Soc. Rev.* **1997**, *26*, 345−354.
(28) Gevorgyan, V.; Rubin, M.; Benson, S.; Liu, J. X. *J. Org. Chem.* **2000**, *65*, 6179−6186.
(29) Parks, D. J.; Piers, W. E. *J. Am. Chem. Soc.* **1996**, *118*, 9440−9441.
(30) Parks, D. J.; Blackwell, J. M.; Piers, W. E. *J. Org. Chem.* **2000**, *65*, 3090−3098.
(31) Gevorgyan, V.; Rubin, M.; Liu, J.-X.; Yamamoto, Y. *J. Org. Chem.* **2001**, *66*, 1672−1675.
(32) Piers, W. E.; Marwitz, A. J. V.; Mercier, L. G. *Inorg. Chem.* **2011**, *50*, 12252−12262.
(33) Hog, D. T.; Oestreich, M. *Liebigs Ann. Chem.* **2009**, *2009*, 5047−5056.
(34) Blackwell, J. M.; Foster, K. L.; Beck, V. H.; Piers, W. E. *J. Org. Chem.* **1999**, *64*, 4887−4892.
(35) Thompson, D. B.; Brook, M. A. *J. Am. Chem. Soc.* **2008**, *130*, 32−33.
(36) Grande, J. B.; Thompson, D. B.; Gonzaga, F.; Brook, M. A. *Chem. Commun.* **2010**, *46*, 4988−4990.
(37) Grande, J. B.; Fawcett, A. S.; McLaughlin, A. J.; Gonzaga, F.; Bender, T. P.; Brook, M. A. *Polymer* **2012**, *53*, 3135−3142.

(38) Kamino, B. A.; Mills, B.; Reali, C.; Gretton, M. J.; Brook, M. A.; Bender, T. P. *J. Org. Chem.* **2012**, *77*, 1663−1674.
(39) Kamino, B. A.; Grande, J. B.; Brook, M. A.; Bender, T. P. *Org. Lett.* **2011**, *13*, 154−157.
(40) Fawcett, A. S.; Grande, J. B.; Brook, M. A. *J. Polym. Sci., Part A: Polym. Chem.* **2013**, *51*, 644−652.
(41) Tan, M.; Zhang, Y. *Tetrahedron Lett.* **2009**, *50*, 4912−4915.
(42) Blackwell, J. M.; Sonmor, E. R.; Scoccitti, T.; Piers, W. E. *Org. Lett.* **2000**, *2*, 3921−3923.
(43) Mountford, A. J.; Lancaster, S. J.; Coles, S. J.; Horton, P. N.; Hughes, D. L.; Hursthouse, M. B.; Light, M. E. *Inorg. Chem.* **2005**, *44*, 5921−5933.
(44) Mountford, A. J.; Hughes, D. L.; Lancaster, S. *J. Chem. Commun.* **2003**, 2148−2149.
(45) Focante, F.; Mercandelli, P.; Sironi, A.; Resconi, L. *Coord. Chem. Rev.* **2006**, *250*, 170−188.
(46) Lešetický, L.; Smrček, S.; Sváta, V.; Podlahová, J.; Podlaha, J.; Císařová, I. *Collect. Czech. Chem. Commun.* **1990**, *55*, 2677−2684.
(47) Evans, B. E. Process for Dibenzocycloheptene Compounds. U.S. Patent 4,235,820, 1980.
(48) Kuzmin, A.; Poloukhtine, A.; Wolfert, M. A.; Popik, V. V. *Bioconjugate Chem.* **2010**, *21*, 2076−2085.
(49) Chadwick, R. C.; Van Gyzen, S.; Liogier, S.; Adronov, A. *Synthesis* **2014**, *46*, 669−677.

dx.doi.org/10.1021/jo501299j | *J. Org. Chem.* 2014, 79, 7728−7733