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Aryl Nitro Reduction with Iron Powder or Stannous Chloride under Ultrasonic Irradiation

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Abstract: The selective reduction of aryl nitro compounds in the presence of sensitive functionalities, including halide, carbonyl, nitrile, and ester substituents, under ultrasonic irradiation at 35 kHz is reported in yields of 39–98%. Iron powder proved superior to stannous chloride with high tolerance of sensitive functional groups and high yields of the desired aryl amines in relatively short reaction times. Simple experimental procedure and purification also make the iron reduction of aryl nitro compounds advantageous over other methods of reduction.

Keywords: iron powder, nitro reduction, ultrasound

Aryl amines are synthetically important compounds that act as precursors to the synthesis of many interesting molecules and can be readily synthesized from aryl nitro compounds via countless reduction methods. The most general methods involve activated metal catalysis[1] and transition-metal-catalyzed hydrogenation,[2] although the latter often employs harsh reaction conditions affecting other reduction-sensitive functionalities such as halides, ketones, aldehydes, esters, and nitriles in addition to the nitro substituent.[2] The selective reduction of aryl nitro compounds using iron powder and dilute acid[3] or stannous chloride[4] have been reported as efficient methods for the synthesis of aryl amines in good yields. However, notable

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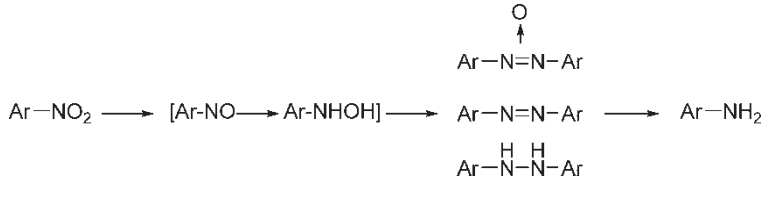
disadvantages to these methods include high reaction temperatures, relatively long reaction times, potential halogenation reactions, and the incompatibility of acid-sensitive functional groups associated with the use of a strong acid such as HCl. The use of milder conditions, for example, acetic acid as solvent, has been reported, but high temperatures and longer reaction times are still evident.[5]

Ultrasound has been reported as an alternative energy source for the initiation of organic reactions,[6] with the potential to accelerate chemical transformations, affect product distributions, improve yields, and increase the catalytic activity of metal particles by factors as high as 10^5.[7] Sonication has been employed in many different types of organic reactions, in particular transition-metal-catalyzed reduction. Generally reactions involving metal reagents exhibit sluggish reaction times due to the presence of surface impurities, but through continuous cleaning and chemical activation of the metal surface and the high temperature and pressure produced by acoustic cavitation, which potentially results in the formation of hot spots,[8a] an accelerated reaction rate is often associated with ultrasound.[7]

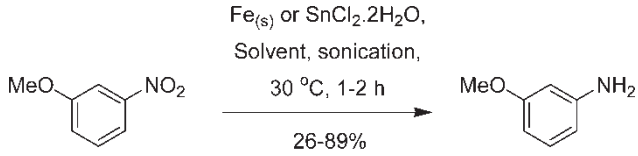
There has been a limited number of aryl nitro reduction procedures via sonication reported in the literature,[8] although a recent study utilizing stannous chloride in the presence of ionic liquids provided aryl amines in good yields.[8a] Other procedures investigated the reduction of nitrobenzene using elemental iron[8b] and reduction of some simple aryl nitro compounds using iron in the presence of multiple additional reagents,[8c] but the tolerance of sensitive functional groups for iron-catalyzed nitro reduction promoted by ultrasound was not examined. The lack of iron and stannous-chloride-catalyzed nitro reduction promoted by ultrasound in the literature prompted the search for more efficient, selective, and relatively straightforward procedures.

The reduction of aryl nitro compounds is known to proceed via the hydroxylamine, followed by azoxy and azo compounds, to its corresponding aryl amine after a prolonged reaction time (Scheme 1).[9] Therefore, the ability of ultrasonic irradiation to accelerate heterogeneous chemical reactions could potentially reduce the reaction time and reduce the amount of intermediates isolated, increasing the yield of aryl amine. To determine the optimal reaction conditions for the reduction of aryl nitro compounds to their corresponding aryl amines under ultrasound conditions without isolation of the intermediates, a series of model reactions were performed (Table 1).



Scheme 1.

Table 1. Investigation of ultrasound-promoted reduction of 3-nitroanisole **1**



1 **2**

Entry	Reducing agent	Solvent	Time (h)	Yield (%)[a]
1	$Fe_{(s)}$ (1 equiv.)	Ethanol/glacial acetic acid/water	2	36
2	$Fe_{(s)}$ (2 equiv.)	Ethanol/glacial acetic acid/water	2	59
3	$Fe_{(s)}$ (5 equiv.)	Ethanol/glacial acetic acid/water	1	89
4	$Fe_{(s)}$ (5 equiv.)	Ethanol/water	2	0
5	$Fe_{(s)}$ (5 equiv.)	Glacial acetic acid/water	1.5	75
6	$SnCl_2 \cdot 2H_2O$ (1 equiv.)	Ethanol	2	26
7	$SnCl_2 \cdot 2H_2O$ (5 equiv.)	Ethanol	2	45
8	$SnCl_2 \cdot 2H_2O$ (10 equiv.)	Ethanol	2	76

[a]Isolated yield.

From these reactions, the optimal conditions were 5 equivalents of iron powder in a mixture of ethanol, glacial acetic acid, and water (2:2:1) exposed to ultrasound for 1 h (entry 3). The reaction was repeated under thermal conditions (2.5 h at 60°C) with the yield of aryl amine **2** determined to be 85%, similar to the optimal conditions in entry 3, but the temperature and time of reaction required for the complete conversion of **1** and its intermediates to **2** were notably higher and longer. This demonstrates that the high-energy effects of acoustic cavitation in addition to the continuous cleaning of the iron surface due to ultrasound are responsible for the enhanced reaction rate. The latter probably accounts for the greatest enhancement in reaction rate because under thermal heating, surface impurities such as oxides, hydroxides, and carbonates inhibit contact between the aryl nitro and the iron surface.[7] In addition, cleansing of the iron sweeps reactive intermediates or products from the surface, making, way for subsequent reactions.[8b]

Entries 1 and 2 demonstrate that the yield of aryl amine **2** decreases significantly as the molar equivalents of iron powder are reduced, probably because of the presence of the intermediates not converted to the aryl amine (Scheme 1), and the yield of **2** was slightly reduced in the absence of ethanol (entry 5). When glacial acetic acid, which presumably helps to

activate the iron powder, is not used in the reaction, no reduction of the aryl nitro was observed (entry 4).

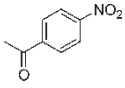
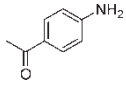
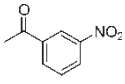
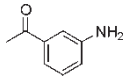
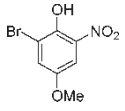
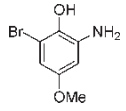
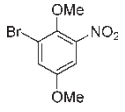
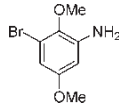
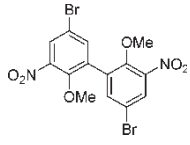
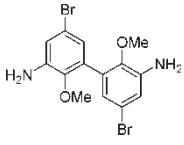
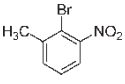
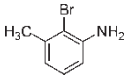
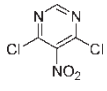
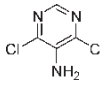
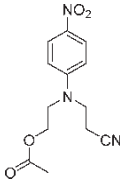
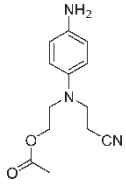
The ability of stannous chloride to selectively reduce an aryl nitro substituent to an aryl amine was also investigated using ethanol as the solvent. Entry 8 demonstrates that for good conversion to the aryl amine, 10 molar equivalents of stannous chloride are required. In the presence of only 1 equivalent (entry 6) and 5 equivalents (entry 7) of stannous chloride, the yields of aryl amine were significantly lower.

The optimal reduction conditions (entry 3) were applied to further nitro aromatic derivatives, examining the selectivity of the reduction for nitro substituents in the presence of other sensitive functionalities (Table 2). Entries 1 to 3 allow comparison between iron- and stannous-chloride-catalyzed reduction, but because of the superiority of iron reduction, entries 4–8 were only performed via this method.

Entries 1 and 2 demonstrate the tolerance of iron reduction for ketone functionalities, which under catalytic hydrogenation conditions could potentially be reduced to their corresponding alcohols and methylene groups.[10] The tolerence of ketone functionalities to iron-catalyzed nitro reduction is well precedented in the literature,[1a,11] and with yields of 77% and 85% for *p*-aminoacetophenone and *m*-aminoacetophenone under ultrasonic irradiation respectively, our conditions also allow complete selectivity for the nitro substituent over the ketone moiety. Both of these compounds have been reported in the literature with yields of 92%[1a] and 80%[12] for the *para*- and *meta*-substituted compounds respectively, and although the former yield is higher than our reported yield, the reaction was done under high pressure at a temperature of 210°C for 2 h with water as solvent. Therefore the iron-catalyzed reduction conditions promoted by ultrasound at 30°C for 1 h are advantageous as they are significantly milder, safer, and easier to perform.

Aryl halides are known to be susceptible to dehalogenation under harsh reduction conditions, in particular catalytic hydrogenation.[2] Entries 3–7 examine the selective reduction of the aryl nitro substituent over the aryl halide, with good to excellent yields obtained in all reactions. Entries 3–6 demonstrate the tolerance of bromine to the optimized iron reduction conditions and, with the exception of entry 3, the yields of desired aryl amine are excellent (86%, 98%, and 85% for entries 4–6 respectively). Although thin-layer chromatography (TLC) showed 100% conversion of 2-bromo-4-methoxy-6-nitrophenol to its corresponding aryl amine (entry 3) with no other intermediates identified, it could only be isolated in 65% yield. During workup, difficulties in isolation of the desired aryl amine were encountered with the product partitioning between both the organic and aqueous phase, therefore contributing to the lower than expected yield. Entry 5 demonstrates the ability of iron-catalyzed reduction under ultrasound to selectively reduce two nitro substituents of a symmetrical dimer with an almost quantitative yield of 98%. The same compound in entry 5 has reportedly been synthesized via iron-catalyzed reduction, in the presence of ferric

Table 2. Reduction of aryl nitro compounds with reduction-sensitive functional groups

Entry	Reagent	Product[b]	$Fe_{(s)}$ rxn. time	Yield using $Fe_{(s)}$ (%)[a]	$SnCl_2 \cdot 2H_2O$ rxn. time	Yield using $SnCl_2 \cdot 2H_2O$ (%)[a]
1			1 h	77	2 h	58
2			1 h	85	2 h	54
3			2 h	65	2 h	35
4			1 h	86	—	—
5			1 h	98[c]	—	—
6			1 h	85	—	—
7			1 h	82	—	—
8			15 min	78	—	—

[a]Isolated yield, 100% conversion, monitored by TLC analysis for completion of the reaction.

[b]Products characterized by ^1H NMR, ^{13}C NMR, and MS and known compounds compared to the literature.

[c]12 Equivalents of iron used.

chloride and concentrated HCl at reflux in ethanol, although it could only be isolated in 69% yield,[13] indicating the superiority of iron-catalyzed reduction promoted by ultrasound. Entry 7 demonstrates the tolerance of chlorine substituents on a pyrimidine ring with a yield of 82% obtained, with previously reported iron-catalyzed reduction reporting a yield of 64%.[14]

Finally, entry 8 was used to examine the tolerance of both an ester and nitrile functionality on an aliphatic chain. The reaction was complete in just 15 min as indicated by TLC analysis and provided the desired aryl amine in 78% yield, demonstrating the ability of ultrasound to drastically accelerate the iron-catalyzed reduction of an aryl nitro functionality in the presence of these reduction-sensitive groups.

In conclusion, an effective and efficient method for the reduction of aryl nitro compounds to their corresponding aryl amine under ultrasonic irradiation has been reported. Although in some instances, marginally higher yields are reported, the reaction of aryl nitro compounds with iron powder in a solvent mixture of ethanol, acetic acid, and water promoted by ultrasonic irradiation provides a much more accessible and simple procedure. Additionally, the short reaction times at relatively low temperature and the use of environmentally benign solvents and cheap reagents make this an attractive and advantageous method for reduction of aryl nitro compounds in organic synthesis.

EXPERIMENTAL

Reagents and solvents used in the experiments were purchased as reagent grade and used without further purification. Sonication was performed in an Elma Transsonic T460 ultrasonic cleaning bath (at a frequency of 35 kHz and a nominal power of 85 W) with all reactions exposed to air in standard glassware or glass sample vials with the temperature of the bath maintained at 30°C. Melting points were determined in a Gallenkamp (Griffin) melting-point apparatus. ^{1}H NMR spectra were acquired on a Varian Unity-300 or Unity-500 spectrometer at 300 MHz and 500 MHz respectively. Spectra were recorded in deuterated chloroform ($CDCl_3$), using chloroform (δ 7.26 ppm) as internal standard. ^{13}C NMR spectra were acquired with a Varian Unity-300 or Unity-500 spectrometer at 76 MHz and 126 MHz respectively using $CDCl_3$ as solvent and chloroform (δ 77.16 ppm) as the internal standard. Electron impact (EI) mass spectra were obtained on a Shimadzu QP-5000 MAT-44 quadrupole spectrometer performed via a direct insertion technique, with an electron beam of 70 eV and a source temperature of less than 200°C, and electrospray ionization (ES) mass spectra were obtained on a VG Quattro-triple quadropole. All data reported for known compounds were spectroscopically identical to those reported in the literature (see compound references).

General Procedure for Nitro Reduction with Iron

To a suspension of **1** (0.147 g, 0.961 mmol) in a mixture of glacial acetic acid (2 mL), ethanol (2 mL), and water (1 mL), was added reduced iron powder (0.279 g, 5.00 mmol). The resulting suspension was exposed to ultrasonic irradiation for 1 h at 30°C with TLC analysis monitoring for the completion of the reaction. The reaction mixture was filtered to remove the iron residue, which was washed with ethyl acetate (30 mL). The filtrate was partitioned with 2M KOH, and the basic layer was further extracted with ethyl acetate (3×25 mL). The combined organic extracts were washed with brine (2×25 mL) and water (3×50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The crude residue was then subjected to flash silica-gel column chromatography (20% ethyl acetate in hexanes), yielding 3-methoxyaniline **2** (89%).

General Procedure for Nitro Reduction with Stannous Chloride

To a solution of **1** (0.148 g, 0.967 mmol) in ethanol (5 mL), was added $SnCl_2 \cdot 2H_2O$ (2.26 g, 10.0 mmol). The reaction mixture was exposed to ultrasonic irradiation for 2 h at 30°C until the reaction was complete as indicated by TLC analysis. The solvent was removed under reduced pressure, and the crude residue was partitioned between ethyl acetate and 2M KOH. The aqueous layer was extracted with further portions of ethyl acetate (3×25 mL), and the combined organic extracts were washed with brine (2×25 mL) and water (3×50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The crude residue was subjected to flash silica-gel column chromatography (20% ethyl acetate in hexanes) yielding 3-methoxyaniline **2** (76%).

Data

3-Methoxyaniline (Table 1)[15]

Dark yellow oil. ^{1}H NMR ($CDCl_3$): δ 7.07 (dd, $J = 8.1$ Hz, 7.8 Hz, 1H); 6.33 (dd, $J = 8.1$ Hz, 2.4 Hz, 1H); 6.30 (dd, $J = 7.8$ Hz, 1.8 Hz, 1H); 6.25 (dd, $J = 2.4$ Hz, 2.4 Hz, 1H); 3.77 (s, 3H); 3.66 (bs, 2H). ^{13}C NMR ($CDCl_3$): δ 160.8, 147.9, 130.2, 108.0, 104.0, 101.1, 55.1. MS (EI) m/z 123 (M, 100%).

p-Aminoacetophenone (Table 2, Entry 1)[16]

Opaque crystalline solid. Mp: 102–103°C (lit.[16] 106–107°C). ^{1}H NMR ($CDCl_3$): δ 7.79 (d, $J = 8.7$ Hz, 2H); 6.63 (d, $J = 9.3$ Hz, 2H); 4.20 (bs,

2H); 2.49 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 196.7, 151.3, 130.9, 127.9, 113.8, 26.2. MS (EI) m/z 135 (M, 60%), 120 (M-15, 100%).

m-Aminoacetophenone (Table 2, Entry 2)[12]

Light bronze solid. Mp: 88–89°C (lit.[12] 98–99°C). ^{1}H NMR ($CDCl_3$): δ 7.31 (ddd, $J = 7.5$ Hz, 1.8 Hz, 1.2 Hz, 1H); 7.25 (dd, $J = 1.8$ Hz, 1.2 Hz, 1H); 7.21 (dd, $J = 8.1$ Hz, 7.5 Hz, 1H); 6.85 (ddd, $J = 8.1$ Hz, 2.1 Hz, 1.2 Hz, 1H); 3.85 (bs, 2H); 2.54 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 198.6, 146.9, 138.3, 129.5, 119.7, 118.9, 114.1, 26.8. MS (EI) m/z 135 (M, 85%), 120 (M-15, 100%).

2-Amino-6-bromo-4-methoxyphenol (Table 2, Entry 3)[17]

Dark brown semisolid. ^{1}H NMR ($CDCl_3$): δ 6.41 (d, $J = 2.7$ Hz, 1H); 6.26 (d, $J = 2.7$ Hz, 1H); 3.70 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 154.3, 136.2, 134.8, 109.8, 105.3, 102.1, 55.9. MS (EI) m/z 217 ($M^{79}Br$, 100%), 219 ($M^{81}Br$, 90%).

3-Bromo-2,5-dimethoxyaniline (Table 2, Entry 4)

Brown viscous oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 6.45 (d, $J = 3.0$ Hz, 1H); 6.23 (d, $J = 2.5$ Hz, 1H); 3.93 (bs, 2H); 3.78 (s, 3H); 3.71 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz): δ 156.9, 141.7, 138.7, 117.1, 107.1, 101.3, 59.9, 55.7. MS (EI) m/z 231 ($M^{79}Br$, 100%), m/z 233 ($M^{81}Br$, 90%). HRMS (EI) calculated for $C_8H_{10}NO_2Br$: 230.9895, found 230.9888.

3,3′-Diamino-5,5′-dibromo-2,2′-dimethoxy-1,1′-biphenyl (Table 2, Entry 5)[13]

Light brown/red crystalline solid. Mp: 172–175°C (lit.[13] 185–186°C). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.89 (d, $J = 2.4$ Hz, 2H); 6.80 (d, $J = 2.1$ Hz, 2H); 3.96 (bs, 4H); 3.44 (s, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 144.0, 141.5, 132.3, 122.8, 118.1, 116.8, 60.1. MS (EI) m/z 400 ($M^{79}Br^{79}Br$, 50%), 402 ($M^{81}Br^{79}Br$, 100%) 404 ($M^{81}Br^{81}Br$, 50%). HRMS (EI) calculated for $C_{14}H_{14}N_2O_2^{79}Br^{79}Br$: 399.9422, found 399.9419.

2-Bromo-3-methylaniline (Table 2, Entry 6)[18]

Yellow oil. ^{1}H NMR ($CDCl_3$): δ 7.00 (dd, $J = 7.8$ Hz, 7.5 Hz, 1H); 6.64 (m, 2H); 3.95 (bs, 2H); 2.39 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 144.4, 138.8, 127.5, 120.38, 113.2, 112.3, 23.7. MS (EI) m/z 238 ($M^{79}Br$, 100%), 240 ($M^{81}Br$, 90%).

5-Amino-4,6-dichloropyrimidine (Table 2, Entry 7)[14]

White solid. ^{1}H NMR ($CDCl_3$): δ 8.21 (s, 1H); 4.50 (bs, 2H). ^{13}C NMR ($CDCl_3$) δ 146.0, 144.3, 136.0. MS (ES+) m/z 164 ($[MH^{35}C1^{35}Cl]^+$, 100%) 166 ($[MH^{37}C1^{35}Cl]^+$, 60%), 168 ($[MH^{37}Cl^{37}Cl]^+$, 10%).

4-Amino-*N*-(1′-cyanoethyl)-*N*-(acetoethyl)aniline (Table 2, Entry 8)

Light brown oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 6.66 (d, $J = 8.9$ Hz, 2H); 6.61 (d, $J = 8.9$ Hz, 2H); 4.12, (t, $J = 5.6$ Hz, 2H); 3.66 (s, 2H); 3.49 (t, $J = 6.1$ Hz, 2H); 3.42 (t, $J = 6.1$ Hz, 2H); 2.46 (t, $J = 6.8$ Hz, 2H); 2.00 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz): δ 171.2, 140.2, 139.5, 118.9, 118.2, 116.9, 62.2, 51.9, 49.2, 21.1, 16.5. MS (ES+) m/z 248 ($[MH]^+$, 100%). HRMS (ES+) calculated for $C_{13}H_{18}N_3O_2$: 248.1399, found 248.1405.

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REFERENCES

1. (a) Wang, L.; Li, P.; Wu, Z.; Yan, J.; Wang, M.; Ding, Y. Reduction of nitroarenes to aromatic amines with nanosized activated metallic iron powder in water. *Synthesis* **2003**, *13*, 2001–2004; (b) Herepoulos, G. A.; Georgakopoulos, S.; Steele, B. R. High intensity ultrasound-assisted reduction of sterically demanding nitroaromatics. *Tetrahedron Lett.* **2005**, *46*, 2469–2473; (c) Nagaraja, D.; Pasha, M. A. Reduction of aryl nitro compounds with aluminium/NH_4Cl: Effect of ultrasound on the rate of the reaction. *Tetrahedron Lett.* **1999**, *40*, 7855–7856; (d) Pyo, S. H.; Han, B. H. Reduction of nitroarenes by activated metals. *Bull. Korean Chem. Soc.* **1995**, *16*, 181–183.
2. (a) Nomura, K. Transition metal catalyzed hydrogenation or reduction in water. *J. Mol. Catal.* **1998**, *130*, 1–28; (b) Downing, R. S.; Kunkeler, P. J.; van Bekkum, H. Catalytic syntheses of aromatic amines. *Catal. Today* **1997**, *37*, 121–136; (c) Boix, C.; Poliakoff, M. Selective reductions of nitroarenes to anilines using metallic zinc in near-critical water. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1487–1490.
3. (a) Liu, Y.; Lu, Y.; Prashad, M.; Repic, O.; Blacklock, T. J. A practical and chemoselective reduction of nitroarenes to anilines using activated iron. *Adv. Synth. Catal.* **2005**, *347*, 217–219; (b) Hazlet, S. E.; Dornfeld, C. A. The reduction of aromatic nitro compounds with activated iron. *J. Am. Chem. Soc.* **1944**, *66*, 1781–1782.
4. Bellamy, F. D.; Ou, K. Selective reduction of aromatic nitro compounds with stannous chloride in nonacidic nonaqueous medium. *Tetrahedron Lett.* **1984**, *25*, 839–842.

5. (a) Guay, V.; Brassard, P. The regiospecific synthesis of the A and B rings of phomazarin. *J. Heterocycl. Chem.* **1987**, *24*, 1649–1652; (b) Owsley, D. C.; Bloomfield, J. J. The reduction of nitroarenes with iron/acetic acid. *Synthesis* **1977**, 118–120.
6. Nuchter, M.; Ondruschka, B.; Jungnickel, A.; Muller, U. Organic processes initiated by non-classical energy sources. *J. Phys. Org. Chem.* **2000**, *13*, 579–586.
7. Luche, J. L. *Synthetic Organic Sonochemistry*; Plenum Press: New York, 1998.
8. (a) Rai, G.; Jeong, J. M.; Lee, Y. S.; Kim, H. W.; Lee, D. S.; Chung, J. K.; Lee, M. C. Ionic liquid mediated efficient reduction of nitroarenes using stannous chloride under sonication. *Tetrahedron Lett.* **2005**, *46*, 3987–3990; (b) Hung, H. M.; Ling, F. H.; Hoffmann, M. R. Kinetics and mechanism of the enhanced reductive degradation of nitrobenzene by elemental iron in the presence of ultrasound. *Environ. Sci. Technol.* **2000**, *34*, 1758–1763; (c) Han, B. H.; Shin, D. H.; Cho, S. Y. Organic sonochemistry: Ultrasonic acceleration of the reduction of aromatic nitro compounds with hydrazine-iron in the presence of activated carbon. *Bull. Korean Chem. Soc.* **1985**, *6*, 320.
9. Pasha, M. A.; Jayashankara, V. P. Reduction of arylnitro compounds to azoarenes and/or arylamines by Al/NaOH in methanol under ultrasonic conditions. *Ultrason. Sonochem.* **2005**, *12*, 433–435.
10. Blaser, H.-U.; Malan, C.; Pugin, B.; Spindler, F.; Steiner, H.; Studer, M. Selective hydrogenation for fine chemicals: Recent trends and new developments. *Adv. Synth. Catal.* **2003**, *345*, 103–151.
11. Radziejewski, C.; Ghosh, S.; Kaiser, E. T. The synthesis of two strongly electron deficient flavin analogs. *Heterocycles* **1987**, *26*, 1227–1238.
12. Simpson, J. C. E.; Atkinson, C. M.; Schofield, K.; Stephenson, O. o-Aminoketones of the acetophenone and benzophenone types. *J. Chem. Soc.* **1945**, 646–657.
13. Viswanathan, N.; Patankar, S. J. Synthesis of 5,5′-dibromo-8,8′-dihydroxy-7,7′-biquinoline. *Indian J. Chem.* **1985**, *24B*, 1284–1285.
14. Baindur, N.; Chadha, N.; Player, M. R. Solution-phase synthesis of a library of 3,5,7-trisubstituted 3*H*-[1,2,3]triazole[4,5-*d*]pyrimidines. *J. Comb. Chem.* **2003**, *5*, 653–659.
15. (a) Lee, D.-Y.; Hartwig, J. F. Zinc trimethylsilylamide as a mild ammonia equivalent and base for the amination of aryl halides and triflates. *Org. Lett.* **2005**, *7*, 1169–1172; (b) Wolter, M.; Nordmann, G.; Job, G. E.; Buchwald, S. L. Copper-catalysed coupling of aryl iodides with aliphatic alcohols. *Org. Lett.* **2002**, *4*, 973–976.
16. Pal, M.; Parasuraman, K.; Yeleswarapu, K. R. Palladium-catalysed cleavage of O/N-propargyl protecting groups in aqueous media under copper-free condition. *Org. Lett.* **2003**, *5*, 349–452.
17. Malamas, M. S.; Manas, E. S.; McDevitt, R. E.; Gunawan, I.; Xu, Z. B.; Collini, M. D.; Miller, C. P.; Dihn, T.; Henderson, R. A.; Keith, J. C., Jr.; Harris, H. A. Design and synthesis of aryl diphenolic azoles as potent and selective estrogen receptor-β ligands. *J. Med. Chem.* **2004**, *47*, 5021–5040.
18. Krolski, M. E.; Renaldo, A. F.; Rudisill, D. E.; Stille, J. K. Palladium-catalysed coupling of 2-bromoanilines with vinylstannanes: A regiocontrolled synthesis of substituted indoles. *J. Org. Chem.* **1988**, *53*, 1170–1176.