

A NOVEL REDUCTION OF AZIDES TO AMINES WITH TELLURIUM METAL IN NEAR-CRITICAL WATER

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Tellurium metal in near-critical water (275°C) provides a novel and efficient method for the reduction of azides, producing amines in good yields.

Keywords: Amines; azides; near-critical water (NCW); reduction; tellurium metal

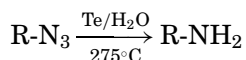
Organic reactions carried out in water have received much more attention in the last decade.¹ Unfortunately most organic compounds are poorly soluble in water at ambient temperature. Nonetheless, the unique properties of water near its critical point ($T_c = 374^\circ\text{C}$, $P_c = 221$ bar) have encouraged researchers to use it instead of organic solvents or ambient temperature water in organic synthesis. As water is heated toward its critical point, it changes from a polar liquid to an almost nonpolar fluid. Its dielectric constant, ϵ , decrease from 78.5 at room temperature to 20 at 275°C , favoring the solubility of organic molecules and ions. Its dissociation constant, K_w , increases several orders of magnitude from ambient to near-critical conditions ($K_w = 10^{-11}$ at 275°C), providing hydronium and hydroxide ions that can act as a modest acid or base in chemical reactions.² Although much of supercritical water research has been focused on the total oxidation of organic

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compounds and geochemical modeling,³ there is an increasing number of papers that suggest near-critical water (250~325°C) can be used as an excellent solvent for organic reactions because organic reactions in near-critical water offer many advantages over those in traditional organic solvents or in supercritical water. For example, it is environmentally benign and the separation of products from reaction mixtures is simplified.⁴

Amines, widely used as important intermediates in the synthesis of dyes, antioxidants and photographic, pharmaceutical and agricultural chemicals can be obtained easily from the reduction of azides with good regio, stereo, and enantioselectivity using catalytic hydrogenation⁵ and a variety of other reducing agents. For example, zinc borohydride,⁶ iodotrimethylsilane,⁷ samarium-iodine,⁸ diboranes,⁹ benzyltriethylammonium tetrathiomolybdate,¹⁰ and hexamethyldisilathiane¹¹ have been recommended for this transformation. However, most of them are carried out in organic solvents, such as CH₃CN, DME, CH₃OH, THF, HMPA, which pose waste handling problems. Recently, Poliakoff reported the selective reduction of nitroarenes to anilines using metallic zinc in near-critical water (250°C).¹² To our knowledge, there is no report so far on the reduction of azides to amines with tellurium metal in water. Here we report a novel reduction of azides by using metallic tellurium powder in near-critical water (NCW) at 275°C, which generate amines in good yields.



RESULTS AND DISCUSSION

Our initial studies were directed toward exploring the reaction conditions for the reduction of azides with metallic tellurium powder in hot water. The results are summarized in Table I. *p*-Methylphenyl azide was chosen as the model compound for this investigation.

As seen from Table I, the reaction temperature has a strong effect on the reduction of *p*-methylphenyl azide with metallic tellurium in hot water. It is evident that *p*-methylphenyl azide could not be reduced to *p*-toluidine with tellurium metal in water at less than 200°C without any additive. Meanwhile, only a smaller yield of reduction product was generated at temperatures between 200 and 250°C. When the reaction temperature has reached ca. 275°C, a good yield of reduction product was obtained. The ratio of tellurium to *p*-methylphenyl azide also was examined. The results show that when the ratio of tellurium to

TABLE I The Reaction Conditions for the Reduction of *p*-Methylphenyl Azide with Tellurium Metal in Water^a

Entry	Te:Azide	Temp. (°C)	Time (h)	Yield (%) ^b
1	3:1	200	4	0 ^c
2	3:1	225	4	19
3	3:1	250	4	52
4	3:1	275	4	90
5	3:1	300	4	89
6	1:1	275	4	43
7	2:1	275	4	71
8	4:1	275	4	90
9	5:1	275	4	89
10	3:1	275	1	34
11	3:1	275	3	77
12	3:1	275	5	88
13	3:1	275	7	85

^aReaction conditions: *p*-methylphenyl azide (1.00 mmol), tap water (10 mL) in a high *T/p* batch reactor system.

^bIsolated yields.

^cStarting material *p*-methylphenyl azide (97%) was recovered.

p-methylphenyl azide is less than 2:1, the reduction was not complete (entries 6 and 7, Table I). As it equals or is higher than 3:1, satisfactory results were achieved (entries 4, 8, and 9, Table I). We also investigated the effect of reaction time on the reduction of *p*-methylphenyl azide and the results indicated that the reaction was not finished when reaction time is less than 3 h (entries 10 and 11, Table I). However, no increase of yield was observed when reaction time is prolonged (entry 13, Table I). The optimized reaction conditions for the reduction of *p*-methylphenyl azide with tellurium metal in water were found to be Te (Eq. 3), *p*-methylphenyl azide (Eq. 1), H₂O (10 mL) at 275°C for 4 h.

We observed that tellurium metal in near-critical water (NCW) at 275°C reduced aryl and alkyl azides efficiently to the corresponding amines in good yields. The reaction was carried out by stirring azide in water with metallic tellurium powder under a nitrogen atmosphere without any organics or additive at 275°C for 4 h. The results are summarized in Table II. As is evident from Table II, the substituent effect for aryl azides has been investigated. The results show that the electronic characteristics of a general electron-donating group (such as CH₃) or a general electron-withdrawing group (such as CH₃CO, Cl) and its location on the aromatic ring were relatively insensitive to the reduction of azides. However, bromo or iodo substituents on the aromatic ring underwent reductive elimination of Br or I in a competitive process, but

TABLE II The Reduction of Azide with Tellurium Metal in Near-Critical Water^a

Entry	Azides	Amines	Yield (%) ^b
1	C ₆ H ₅ N ₃	C ₆ H ₅ NH ₂	82
2	<i>p</i> -CH ₃ C ₆ H ₄ N ₃	<i>p</i> -CH ₃ C ₆ H ₄ NH ₂	88
3	<i>m</i> -CH ₃ C ₆ H ₄ N ₃	<i>m</i> -CH ₃ C ₆ H ₄ NH ₂	86
4	<i>m</i> -CH ₃ COC ₆ H ₄ N ₃	<i>m</i> -CH ₃ COC ₆ H ₄ NH ₂	89
5	<i>p</i> -ClC ₆ H ₄ N ₃	<i>p</i> -ClC ₆ H ₄ NH ₂	90
6	<i>p</i> -BrC ₆ H ₄ N ₃	<i>p</i> -BrC ₆ H ₄ NH ₂	32 ^c
		C ₆ H ₅ NH ₂	40 ^c
7	<i>m</i> -ClC ₆ H ₄ N ₃	<i>m</i> -ClC ₆ H ₄ NH ₂	80
8	<i>n</i> -C ₁₂ H ₂₅ N ₃	<i>n</i> -C ₁₂ H ₂₅ NH ₂	87
9	<i>n</i> -C ₁₆ H ₃₃ N ₃	<i>n</i> -C ₁₆ H ₃₃ NH ₂	91
10	<i>p</i> -IC ₆ H ₄ N ₃	C ₆ H ₅ NH ₂	70
11	<i>o</i> -HO ₂ CC ₆ H ₄ N ₃	C ₆ H ₅ NH ₂	72
12	α -C ₁₀ H ₇ N ₃	α -C ₁₀ H ₇ NH ₂	92

^aReaction conditions: azide (1.00 mmol), tellurium metal (3.00 mmol), tap water (10 mL) in a high *T/p* batch reactor system at 275°C for 4 h.

^bIsolated yields.

^cDetermined by GC and NMR analysis of the reaction mixture.

a chloro substituent remained unchanged. The reactivity of halogen atoms on the aromatic ring is I > Br > Cl, which is consistent with the expected reactivity and Poliakoff's experimental results.¹² A carboxylic group on the aromatic ring also underwent a decarboxylation reaction, along with the reduction process.

In conclusion, a novel, reliable, and practical procedure for the preparation of amines has been developed which involves the use of tellurium metal as reductive agent and azides as starting material in near-critical water. The method has the advantages of simple operation, good chemoselectivity, and use of an inexpensive, nontoxic, nonflammable solvent. It may be a new way for the application of tellurium metal directly in organic synthesis.

EXPERIMENTAL

Melting points were recorded on a WRS-1A melting point apparatus and are uncorrected. ¹H NMR spectra were recorded on a 300 MHz Bruker AZ 300 spectrometer. Chemical shifts are given as δ value with reference to tetramethylsilane (TMS) as internal standard. IR spectra were obtained by using a Nicolet NEXUS 470 spectrophotometer. The

reagents were used as received from a commercial supply without purification prior to use.

General procedure for the reduction of azides with metallic tellurium in near-critical water:

Azide (1.00 mmol) and metallic tellurium powder (383 mg, 3.00 mmol) were added to a high temperature and pressure stainless steel reactor charged with tap water (10 mL) under a nitrogen atmosphere, with stirring. The reactor was heated at 275°C for 4 h. After cooling, diethyl ether (10 mL \times 2) was added to extract the products. After the organic layer was dried with anhydrous sodium sulfate, the solvents were evaporated under reduced pressure. The product was purified by flash chromatography to yield amine.

Aniline. Oil.¹³ $^1\text{H NMR}$ (CDCl_3): δ 7.23 (t, 2H, $J = 8.6$ Hz), 6.78 (m, 3H), 3.58 (s, 2H). IR (film): ν_{max} 3460, 3362, 1600, 1495 cm^{-1} . (Found: C, 77.09; H, 7.79; N, 15.12; $\text{C}_6\text{H}_7\text{N}$ requires: C, 77.38; H, 7.58; N, 15.04).

***p*-Methylaniline.** m.p. 43–45°C (lit.¹⁴ 44–46°C). $^1\text{H NMR}$ (CDCl_3): δ 6.98 (d, 2H, $J = 8.2$ Hz), 6.62 (d, 2H, $J = 8.3$ Hz), 3.42 (s, 2H), 2.28 (s, 3H). IR (KBr): ν_{max} 3426, 3325, 1609, 1508 cm^{-1} . (Found: C, 78.63; H, 8.58; N, 12.79; $\text{C}_7\text{H}_9\text{N}$ requires: C, 78.46; H, 8.47; N, 13.07).

***p*-Chloroaniline.** m.p. 67–69°C (lit.¹⁵ 68–70°C). $^1\text{H NMR}$ (CDCl_3): δ 7.04 (d, 2H, $J = 8.5$ Hz), 6.72 (d, 2H, $J = 8.4$ Hz), 3.40 (s, 2H). IR (KBr): ν_{max} 3470, 3412, 1600, 1504 cm^{-1} . (Found: C, 56.23; H, 4.86; N, 11.21; $\text{C}_6\text{H}_6\text{ClN}$ requires: C, 56.49; H, 4.74; N, 10.98).

***p*-Bromoaniline.** m.p. 62–64°C (lit.¹⁶ 62–64°C). $^1\text{H NMR}$ (CDCl_3): δ 7.23 (d, 2H, $J = 8.6$ Hz), 6.57 (d, 2H, $J = 8.5$ Hz), 3.65 (s, 2H). IR (KBr): ν_{max} 3456, 3365, 1614, 1488 cm^{-1} . (Found: C, 42.03; H, 3.25; N, 8.29; $\text{C}_6\text{H}_6\text{BrN}$ requires: C, 41.89; H, 3.52; N, 8.14).

***m*-Methylaniline.** Oil. b.p. 199–201°C (lit.¹⁷ 200–202°C). $^1\text{H NMR}$ (CDCl_3): δ 7.02 (m, 1H), 6.56 (t, 1H, $J = 8.1$ Hz), 6.42 (m, 2H), 3.57 (s, 2H), 2.32 (s, 3H). IR (film): ν_{max} 3416, 3335, 1605, 1503 cm^{-1} . (Found: C, 78.18; H, 8.59; N, 13.23; $\text{C}_7\text{H}_9\text{N}$ requires: C, 78.46; H, 8.47; N, 13.07).

***m*-Chloroaniline.** Oil. b.p. 220–222°C (lit.¹⁸ 223°C). $^1\text{H NMR}$ (CDCl_3): δ 7.04 (m, 1H), 6.72 (t, 1H, $J = 7.2$ Hz), 6.64 (s, 1H), 6.48 (m, 1H), 3.42 (s, 2H). IR (film): ν_{max} 3456, 3405, 1612, 1514 cm^{-1} . (Found: C, 56.72; H, 4.61; N, 10.74; $\text{C}_6\text{H}_6\text{ClN}$ requires: C, 56.49; H, 4.74; N, 10.98).

***m*-Acetylaniline.** m.p. 92–94°C (lit.¹⁹ 92–93°C). $^1\text{H NMR}$ (CDCl_3): δ 7.24 (t, 1H, $J = 7.7$ Hz), 7.08 (m, 2H), 6.68 (m, 1H), 3.62 (s, 2H), 2.59 (s, 3H). IR (KBr): ν_{max} 3446, 3354, 1659, 1612, 1489 cm^{-1} . (Found: C, 70.86; H, 6.87; N, 10.55; $\text{C}_8\text{H}_9\text{NO}$ requires: C, 71.09; H, 6.71; N, 10.36).

***1*-Naphthalenamine.** m.p. 47–48°C (lit.²⁰ 48–49°C). $^1\text{H NMR}$ (CDCl_3): δ 7.82 (m, 2H), 7.38 (m, 2H), 7.15 (m, 2H), 6.67 (d, 1H, $J = 8.0$ Hz), 3.55 (s, 2H). IR (KBr): ν_{max} 3458, 3365, 1607, 1502 cm^{-1} . (Found: C, 83.59; H, 6.47; N, 9.94; $\text{C}_{10}\text{H}_9\text{N}$ requires: C, 83.88; H, 6.34; N, 9.78).

1-Dodecylamine. m.p. 28–29°C (lit.²¹ 28°C). ¹H NMR (CDCl₃): δ 2.65 (t, *J* = 2.06 Hz, 2H), 2.35 (s, 2H), 1.55–1.30 (m, 20H), 0.89 (t, *J* = 6.80 Hz, 3H). IR (film): ν_{\max} 3458, 3365, 1380 cm⁻¹. (Found: C, 77.85; H, 14.75; N, 7.40; C₁₂H₂₇N requires: C, 77.76; H, 14.68; N, 7.56).

1-Hexadecanamine. m.p. 45–47°C (lit.²² 47°C). ¹H NMR (CDCl₃): δ 2.68 (t, *J* = 2.10 Hz, 2H), 2.40 (s, 2H), 1.57–1.29 (m, 28H), 0.90 (t, *J* = 6.90 Hz, 3H). IR (KBr): ν_{\max} 3462, 3360, 1380 cm⁻¹. (Found: C, 79.82; H, 14.47; N, 5.71; C₁₆H₃₅N requires: C, 79.59; H, 14.61; N, 5.80).

Safety Warning: This procedure involves a high temperature and pressure and only must be carried out in an apparatus with the appropriate pressure rating at the reaction temperature. It also should be performed in a safe place.

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