

Scalable Synthesis of Pure and Stable Hexaaminobenzene Trihydrochloride

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Abstract: Synthesis of hexaaminobenzene (HAB) in pure and stable form has remained as an important challenge for a long time, since it is a fascinating synthon for the synthesis of aromatic nitrogenous compounds having many interesting applications. Here, we report an improved synthesis of pure and stable HAB form using modified catalytic hydrogenation in aqueous acidic medium. The structure of needle-shaped HAB crystals was confirmed by single-crystal X-ray diffraction study. The synthetic protocol could thus be a simple, but efficient for the large-scale synthesis of highly pure and stable HAB.

Key words: hexaaminobenzene, palladium, reduction, TATB, TNA

The usefulness of the hexaaminobenzene (HAB) can be imagined on the basis of the new type of polynitrogenous heterocyclic systems including derivatives of hexaazatriphenylene,^{1,2} hexaazacoronene,³ fused benzotriazoles,⁴ benzotris(imidazole),^{5,6} benzotris[1,2,5]thiadiazole,⁷ benzotris[1,2,5]selenodiazole,⁷ aromatic hexaamides with the properties of lyotropic liquid crystals,⁴ and many other interesting materials.^{8–10} This interesting symmetric compound has been known to synthetic community for many decades.¹¹ There have been many attempts to synthesize HAB by reducing 1,3,5-triamino-2,4,6-trinitrobenzene (TATB) with phenylhydrazine,² catalytic hydrogenation,³ and sodium in liquid ammonia,¹ which are commonly used methods. In all these cases, the HAB obtained is in the form of free amine, which is highly sensitive to oxygen and light, decomposed into dark brown amorphous product both in diffuse daylight and in the dark within a few hours even under the argon atmosphere.^{3,12,13} Although HAB trihydrochloride has been envisaged in one step in an aqueous HCl solution in the presence of SnCl₂,⁴ its purity and stability is still not satisfactory. Hitherto, there have thus been no reasonably feasible reports for the large-scale synthesis of highly pure HAB trihydrochloride crystals in an efficient way, due mainly to the instability of HAB. As a result, the most reported methods have directly used HAB for subsequent reactions without purification to remove reduction catalyst and possible impurities, if any.^{1,3}

We surveyed different literature procedures to obtain highly pure HAB by using a variety of conventional methods involving the reduction of aromatic nitro groups on

TATB (Figure 1, a). Although some quantity of HAB was produced by using literature-reported methods with poor quality in very low yield (Figure 1, b), all cases have failed during the catalyst removal and purification. The extremely poor stability of free HAB was the major contributing factor by judging its white color rapidly turning into dark brown. Kohne et al. have reported the synthesis of HAB trihydrochloride crystals.¹³ However, the procedure is tedious, time-consuming, and requires extreme care. Any minor mistake can ruin the whole effort, and thus obtaining pure HAB in large scale has been almost impossible. Nevertheless, the quality of HAB trihydrochloride crystals is the best among reported methods, although it is still unsatisfactory (Figure 1, c). After repeated failures to synthesize highly pure HAB crystals, we have now optimized a new and convenient procedure for the synthesis of this fragile compound in a stable form by using a modified catalytic reduction.

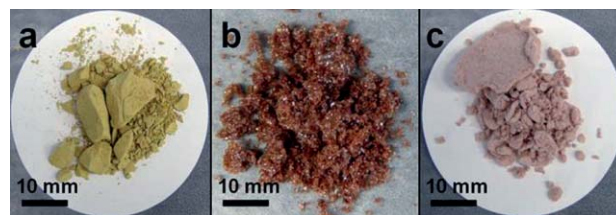
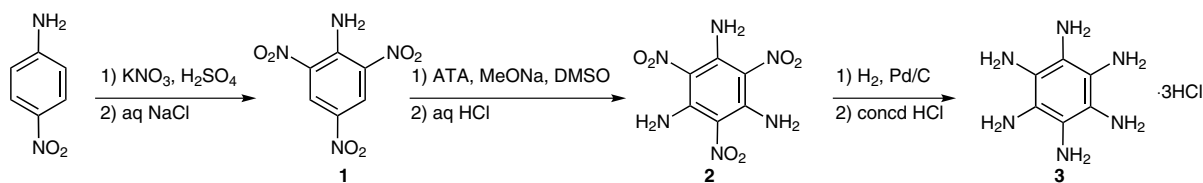


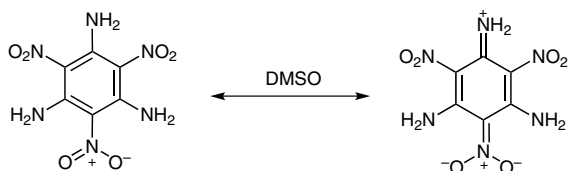
Figure 1 (a) TATB; (b) HAB crystals as one of the best obtained samples from conventional catalytic reduction of TATB in the presence of H₂ and palladium (10 wt%) on activated carbon (Pd/C);³ (c) HAB trihydrochloride crystals obtained from the reduction of TATB in the presence of SnCl₂/HCl system.⁴

The overall synthesis started with the well-known nitration of *p*-nitroaniline into 2,4,6-trinitroaniline in concentrated sulfuric acid in the presence of potassium nitrate (Scheme 1).¹⁴ The purified 2,4,6-trinitroaniline was treated with 4-amino-1,2,4-triazole (ATA) and sodium methoxide in dimethyl sulfoxide (DMSO) under vicarious nucleophilic reaction conditions, and subsequent acid quenching with 0.4 M HCl produced 1,3,5-triamino-2,4,6-trinitrobenzene (TATB) in high yield.¹⁵ Interestingly, the TATB in DMSO displays a mesomeric form to relieve some of its strain by delocalizing its lone-pair electron into the aromatic ring (Scheme 2). ¹³C NMR confirms the proposed mesomerism in TATB.

Finally, the TATB was reduced to form HAB trihydrochloride by a modified procedure to give highly pure creamy white needlelike crystals (Figure 2, a), highly



Scheme 1 The synthesis of HAB trihydrochloride



Scheme 2 Mesomerism of TATB in DMSO

transparent and reflective (Figure 2, b), indicating the high quality of crystals. Crystal-length dimensions are longer than 1 mm (Figure 2, c) and some are even longer than 5 mm from the optical microscope image. The crystals are stable in a closed vial since five months (Figure 2, d). The absolute crystal structure of HAB trihydrochloride has been solved for the first time by single-crystal X-ray diffraction analysis (Figure 2, e and f, see also items S1–S3 in the Supporting Information). Hence, the large-scale synthesis of pure HAB trihydrochloride crystals was achieved by an optimized synthetic procedure (see details in the experimental section). All substituted aromatic nitro compounds should be handled with care because of their explosive nature, but we did not face any such accident in our extended experimental work.

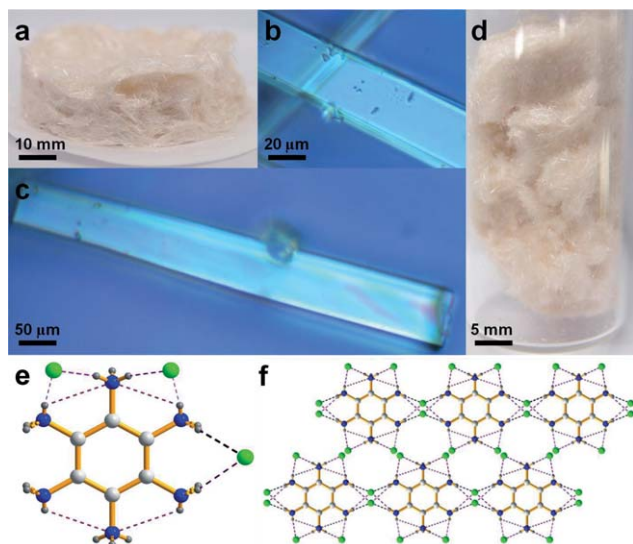


Figure 2 (a) Digital photograph of HAB trihydrochloride crystals on PTFE filter membrane; (b), (c) optical microscopic images of the HAB trihydrochloride crystals; (d) digital photograph of HAB in vial after five months; (e) a ball-and-stick diagram of formula unit of the HAB trihydrochloride; (f) hydrogen-bonding-driven molecular packing viewed along the crystallographic *c* axis, where the hydrogen bonds were represented using dotted lines. Color codes: carbon, gray; hydrogen, dark gray; nitrogen, blue; chloride, green.

The density of electrons on the HAB is extremely high, because of the presence of six strong electron-donating NH_2 groups around the aromatic benzene ring, which makes this compound highly reactive and unstable in its free form (base). To reduce the electronic density by push–pull mechanism, we converted it into its hydrochloride salt form, which reduces the electronic density to some extent but it is still very reactive when it is in the dissolved state. The HAB could be a fascinating building block for the synthesis of discotic liquid crystals,^{16–19} compounds with low barrier to both electron and hole transport for potential applications in organic electronics,²⁰ synthesis of macrocyclic compounds,²¹ hexaazatriphenylene-based donor–acceptor molecules,^{8,22} electron-deficient expanded-electron systems,²³ ferromagnetic organic salts,^{3,24} and fluorescence sensor for cadmium(II).²⁵

In summary, we have the strong hunch that our method would be equally useful for the synthesis of other sensitive aromatic amines from their parent polynitroarenes. Albeit the modified reduction method reported here has not been tested on other polynitroarene compounds, it would be of great interest for the reduction of other sensitive compounds with this newly developed method. Furthermore, pure HAB could be an important building block for the synthesis of many aesthetic and application-specific compounds.

Solvents, chemicals, and reagents were purchased from Aldrich Chemical Inc., unless otherwise stated. Reactions were performed under nitrogen or argon atmosphere using oven-dried glassware. 2,4,6-Trinitroaniline¹⁴ and 1,3,5-triamino-2,4,6-trinitrobenzene¹⁵ were synthesized according to the literature. 4-Nitroaniline (185310) 99%, DMSO (276855) 99.9%, Pd/C 10% (75990), HCl 37% (435570), and EtOAc (anhyd) were purchased from Sigma-Aldrich Chemical Inc. Nitric acid 60% (010223) was purchased from DC Chemical Co. Ltd. Celite 545 (C0340) was provided by Samchun Pure Chemical Co. Ltd.

Infrared (FT-IR) spectra were recorded on a Perkin-Elmer Spectrum 100 FT-IR spectrophotometer. Single-crystal X-ray diffraction data were taken on R-Axis RAPID II (Rigaku, Japan). ¹H NMR and ¹³C NMR spectra were taken by using a FT-NMR 600 MHz VNMRS 600 (Varian, USA) spectrometer. Mass spectra were recorded on a 320-MS Varian, USA. Elemental analysis was carried out on Flash 2000 Thermo Scientific, Netherland. Hydrogenation was carried out using shaker-type Parr Hydrogenation Apparatus Model-3911. Melting points were calculated on KSP1N automatic melting point meter (A. Krüss Optronic GmbH, Germany).

Synthesis of TNA (1)

4-Nitroaniline (20 g, 0.088 mol) and H_2SO_4 (100 mL) were charged in a round-bottom flask. A solution of KNO_3 (70 g, 0.70 mol) in H_2SO_4 (100 mL) was then added dropwise at 50 °C. The mixture was heated to 80 °C for 3 h and 110 °C for 3 h. After completion of

the reaction, the reaction mixture was cooled to ambient temperature and poured into ice water. The precipitates were collected by suction filtration, air-dried, and recrystallized from very dilute aq HCl solution to give 16.5 g (50% yield) of 2,4,6-trinitroaniline (glassy light yellow crystal); mp 186–188 °C (lit.¹⁴ 188 °C). MS (EI, DIP): m/z (%) = 229 (100) $[M + H]^+$. Anal. Calcd (%) for $C_6H_4N_4O_6$ (228.12): C, 31.59; H, 1.77; N, 24.56; O, 42.08. Found: C, 30.51; H, 1.30; N, 20.70; O, 43.86. ¹H NMR (600 MHz, DMSO): δ = 8.59 (2 H), 5.60 (2H) ppm. ¹³C NMR (600 MHz, DMSO, S6): δ = 141.86 (C-4), 125.27 (C-2), 124.55 (C-3), 160.62 (C-1) ppm. See also items S4–S6 in the Supporting Information.

Synthesis of TATB (2)

NaOMe (23.8 g, 0.44 mol) was added to a solution of TNA (4.56 g, 0.02 mol) and ATA (16.8 g, 0.2 mol) in DMSO (300 mL). The reddish-orange suspension was stirred at ambient temperature for 3 h. The reaction mixture was then poured into cold aq HCl (0.4 M) solution. The resulting precipitates were collected by suction filtration, washed with distilled H₂O and dried. The solid was dissolved in DMSO with small amount of NaOH with gentle heating up to 70 °C, when the compound was completely dissolved the solution was poured into ice-cold aq HNO₃ (0.4 M) solution. The product precipitated was again collected by filtration to give 4.62 g (89% yield) of TATB (deep bright yellow powder); mp >300 °C (dec.) [lit.² >300 °C (dec.)]. MS (EI, DIP, S7): m/z (%) = 259.1 (100) $[M + H]^+$. Anal. Calcd (%) for $C_6H_6O_6N_6$ (258.14): C, 27.9; H, 2.32; N, 32.55; O, 37.2. Found: C, 28.03; H, 1.86; N, 26.57; O, 44.79. ¹³C NMR (600 MHz, DMSO, S8): 113.52 (C-4), 117.48 (C-2), 147.01 (C-3), 157.14 (C-1). The FT-IR spectrum shows an asymmetrical N–H stretching absorption peak at 3363 cm⁻¹ and a symmetrical N–H stretching vibration at 3225 cm⁻¹, which are characteristic peaks for TATB. Other peaks are N–O asymmetrical stretching at 1560 cm⁻¹, symmetrical N–O stretching at 1201 cm⁻¹, C–N stretching (amino group) 1613 and 798 cm⁻¹, and skeletal stretching of the ring at 1475, 1180, 1053 cm⁻¹. See also items S7 and S8 in the Supporting Information.

Synthesis of HAB (3)

TATB (3.0 g, 0.012 mol) was taken in a high-pressure hydrogenation bottle with 10% Pd/C (500 mg) and pure EtOAc (150 mL) as a solvent. The reaction flask was placed and fixed on hydrogenation apparatus and agitated under H₂ (4.2 bar) until all the yellowish color of the reactant disappeared completely within 3 d. Then, concentrated HCl (90 mL) was added, and the reaction was continued under H₂ for an additional 5 h. The reaction mixture was filtered under reduced pressure over Celite to remove catalyst. The HAB trihydrochloride crystallized out very nicely (see item S9 in the Supporting Information) in high yield. The precipitates were collected by suction filtration by using polytetrafluoroethylene (PTFE) membrane (0.5 μ m pore) and dried in an oven at 70 °C for 4 h under reduced pressure (6.6·10⁻⁴ bar). The white small crystals were redissolved in deionized H₂O and filtered through PTFE membrane to remove solid impurities, if any, and added 80 mL of concentrated HCl. The flask was tightly sealed and placed in the freezer until very nice big crystals developed. The crystals were collected on PTFE membrane filter in the room environment and washed thoroughly with EtOAc and dried in the vacuum oven (Figure 2, a) to afford 3.0 g (92% yield). HAB trichloride shows no melting point but becomes dark at above 250 °C. (lit.¹¹ >240 °C darken). MS (EI, DIP): m/z (%) = 169.1 (78.5) $[M + H]^+$, 167.1 (100) $[M - H]^+$. Anal. Calcd (%) for $C_6H_{15}N_6Cl_3$ (277.58): C, 25.96; Cl, 38.32; H, 5.45; N, 30.28. Found: C, 26.54; Cl, 36.54; H, 4.96; N, 25.05; O, 6.89. FT-IR: 3384.41, 3249.28, 2977.06, 2564.72, 1671.16, 1636, 1582.02, 1554, 1479.74, 1279, 1202.9, 1166.34, 1096 cm⁻¹. See also item S10 in the Supporting Information.

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Supporting Information for this article is available online at <http://www.thieme-connect.com/ejournals/toc/synlett>.

References

- Rogers, D. Z. *J. Org. Chem.* **1986**, *51*, 3904.
- Kohne, B.; Praefcke, K. *Liebigs Ann. Chem.* **1985**, 522.
- Breslow, R.; Maslak, P.; Thomaidis, J. S. *J. Am. Chem. Soc.* **1984**, *106*, 6453.
- Khislamutdinov, G. K.; Korolev, V. L.; Kondyukov, I. Z.; Abdrakhmanov, I. S.; Smirnov, S. P.; Fainzilberg, A. A.; Dorokhov, V. G. *Russ. Chem. Bull.* **1993**, *42*, 136.
- Kohne, B.; Praefcke, K.; Derz, T.; Gondro, T.; Frolow, F. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 650.
- Wolff, J. J.; Limbach, H.-H. *Liebigs Ann. Chem.* **1991**, 691.
- Praefcke, K.; Kohne, B.; Korinath, F. *Liebigs Ann. Chem.* **1990**, 203.
- Juárez, R.; Ramos, M.; Segura, J. L.; Orduna, J.; Villacampa, B.; Alicante, R. *J. Org. Chem.* **2010**, *75*, 7542.
- Ishi-i, T.; Murakami, K.-I.; Imai, Y.; Mataka, S. *J. Org. Chem.* **2006**, *71*, 5752.
- Ishi-i, T.; Murakami, K.-I.; Imai, Y.; Mataka, S. *Org. Lett.* **2005**, *7*, 3175.
- Flurschheim, B.; Holmes, E. L. *J. Chem. Soc.* **1929**, 330.
- Thomaidis, J.; Maslak, P.; Breslow, R. *J. Am. Chem. Soc.* **1988**, *110*, 3970.
- Kohne, B.; Praefcke, K. *Liebigs Ann. Chem.* **1987**, 265.
- You, B. W.; Bo, Z. W.; Zhi, H. Y.; Yan, S.; Hui, Q. *Chin. J. Energ. Mater.* **2011**, *19*, 142.
- Mitchell, A. R.; Pagoria, P. F.; Schmidt, R. D. US 5633406, **1997**.
- Ong, C. W.; Liao, S.-C.; Chang, T. H.; Hsu, H.-F. *Tetrahedron Lett.* **2003**, *44*, 1477.
- Yeh, M.-C.; Liao, S.-C.; Chao, S.-H.; Ong, C. W. *Tetrahedron* **2010**, *66*, 8888.
- Ong, C. W.; Liao, S.-C.; Chang, T. H.; Hsu, H.-F. *J. Org. Chem.* **2004**, *69*, 3181.
- Ishi-i, T.; Hirayama, T.; Murakami, K.-i.; Tashiro, H.; Thiemann, T.; Kubo, K.; Mori, A.; Yamasaki, S.; Akao, T.; Tsuboyama, A.; Mukaide, T.; Ueno, K.; Mataka, S. *Langmuir* **2005**, *21*, 1261.
- Barlow, S.; Zhang, Q.; Kaafarani, B. R.; Risko, C.; Amy, F.; Chan, C. K.; Domercq, B.; Starikova, Z. A.; Antipin, M. Y.; Timofeeva, T. V.; Kippelen, B.; Brédas, J.-L.; Kahn, A.; Marder, S. R. *Chem.-Eur. J.* **2007**, *13*, 3537.
- Secondo, P.; Fages, F. *Org. Lett.* **2006**, *8*, 1311.
- Juárez, R.; Ramos, M. M.; Segura, J. L. *Tetrahedron Lett.* **2007**, *48*, 8829.
- Ishi-i, T.; Hirashima, R.; Tsutsumi, N.; Amemori, S.; Matsuki, S.; Teshima, Y.; Kuwahara, R.; Mataka, S. *J. Org. Chem.* **2010**, *75*, 6858.
- Breslow, R.; Jaun, B.; Kluttz, R. Q.; Xia, C.-Z. *Tetrahedron* **1982**, *38*, 863.
- Zhao, Q.; Li, R.-F.; Xing, S.-K.; Liu, X.-M.; Hu, T.-L.; Bu, X.-H. *Inorg. Chem.* **2011**, *50*, 10041.